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# Toxicological Profile for Chrysene

ICF-Clement, Washington, DC

Prepared for:

Agency for Toxic Substances and Disease Registry, Atlanta, GA

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# Toxicological Profile for

# CHRYSENE

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

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This report was prepared as required by section 110 (3) of the Superfund Amendments and Reauthorization Act of 1986 (42 U.S.C. 9618(f)

16. Abstract (Limit: 200 words)

The ATSDR Toxicological Profile for Chrysene is intended to characterize succinctly the toxicological and health effects information for the substance. It identifies and reviews the key literature that describes the substances's toxicological properties. Other literature is presented but described in less detail. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced. The profile begins with a public health statement, which describes in nontechnical language the substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine the substance's health effects is described. Research gaps in nontoxic and health effects information are described. Research gaps that are of significance to the protection of public health will be identified in a separate effort. The focus of the document is on health and toxicological information.

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## FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 100 most significant hazardous substances was published in the *Federal Register* on April 17, 1987.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> "(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Research gaps in toxicologic and health effects information are described in the profile. Research gaps that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents in response to public comments and as additional data become available; therefore, we encourage comment that will make the toxicological profile series of the greatest use.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

James O. Mason

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Assistant Surgeon General
Administrator, ATSDR

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# 1. PUBLIC HEALTH STATEMENT

## 1.1 WHAT IS CHRYSENE?

Chrysene is one of the polycyclic aromatic hydrocarbon (PAH) compounds. Because it is formed when gasoline, garbage, or any animal or plant material burns, it is usually found in smoke and soot. This chemical combines with dust particles in the air and is carried into water and soil and onto crops. Chrysene is found in the coal tar pitch that industry uses to join electrical parts. It is also found in creosote, a chemical used to preserve wood.

## 1.2 HOW MIGHT I BE EXPOSED TO CHRYSENE?

People may be exposed to chrysene from environmental sources such as air, water, and soil and from cigarette smoke and cooked food. Workers who handle or are involved in the manufacture of PAH-containing materials may also be exposed to chrysene. Typically, exposure for workers and the general population is not to chrysene alone but to a mixture of similar chemicals.

The general population may be exposed to dust, soil, and other particles that contain chrysene. The largest sources of chrysene in the air are open burning and home heating with wood and coal. Factories that produce coal tar also contribute small amounts of chrysene to the air. People may come in contact with chrysene from soil on or near hazardous waste sites, such as former gas-manufacturing sites or abandoned wood-treatment plants that used creosote. At this time, chrysene has been found at 71 out of 1,177 sites on the National Priorities List (NPL) of hazardous waste sites in the United States. As more sites are evaluated by the Environmental Protection Agency (EPA), this number could change. The soil near areas where coal, wood, or other products have been burned is another source of exposure. Exposure to chrysene and other PAHs may also occur through skin contact with products that contain PAHs such as creosote-treated wood, asphalt roads, or coal tar.

People may be exposed to chrysene by drinking water from the drinking water supplies in the U.S. that have been found to contain low levels of the chemical. Foods grown in contaminated soil or air may contain chrysene. Cooking food at high temperatures, as occurs during charcoal-grilling or charring, can increase the amount of chrysene in the food. Chrysene has been found in cereals, vegetables, fruits, meats, beverages, and in cigarette smoke.

The greatest exposure to chrysene is likely to take place in the workplace. People who work in coal tar production plants; coking plants; asphalt production plants; coal-gasification sites; smoke houses; municipal trash incinerators; and facilities that burn wood, coal, or oil may be exposed to chrysene in the workplace air. Chrysene may also

be found in areas where high-temperature food fryers and broilers are used.

### 1.3 HOW DOES CHRYSENE GET INTO MY BODY?

The most common way chrysene enters the body is through the lungs when a person breathes in air or smoke containing it. It also enters the body through the digestive system when substances containing it are swallowed. Although chrysene does not normally enter the body through the skin, small amounts could enter if contact occurs with soil that contains high levels of chrysene (for example, near a hazardous waste site) of if contact is made with heavy oils containing chrysene.

### 1.4 HOW CAN CHRYSENE AFFECT MY HEALTH?

Chrysene causes cancer in laboratory animals when applied to their skin. This finding suggests that it is likely that people exposed in the same manner could also develop cancer.

Because studies of chrysene are not complete, we don't know if chrysene that is breathed in or swallowed could cause cancer or if it can cause harmful effects other than cancer.

### 1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO CHRYSENE?

Very few tests are available that can tell if exposure to chrysene has taken place. In the body, chrysene is changed to related chemical substances called metabolites. The metabolites can bind with DNA, the genetic material of the body. The body's response after exposure can be measured in the blood. However, this test is still being developed. Chrysene can also be found in the urine of individuals exposed to PAHs. It is not possible to know from these tests how much chrysene a person was exposed to or to predict what health effects may happen at certain levels. Also, none of these tests have been used in exposure situations outside the workplace.

### 1.6 WHAT LEVELS OF CHRYSENE EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

No information has been found about specific levels of chrysene that have caused harmful effects in people after breathing, swallowing, or touching the substance.

Skin cancer has developed in mice that had chrysene on their skin throughout their lives. Skin cancer is the only harmful effect that can be predicted when animals are exposed to chrysene. It is not known if similar levels could cause cancer in people. No information has been found about harmful effects of chrysene in animals that breathed in or ate the chemical.

### 1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

Based on information from another PAH chemical, the federal government has developed standards and guidelines to protect individuals from the potential health effects of PAHs, including chrysene, in

drinking water. EPA has provided estimates of levels of total cancer-causing PAHs in lakes and streams associated with various risks of developing cancer in people. EPA has also determined that any release of PAHs of more than 1 pound should be reported to the National Response Center.

Pure chrysene is produced in the United States only as a laboratory chemical. However, chrysene is a PAH, and PAHs are found in coal tar and in the creosote oils and pitches formed from the production of coal tar. The government's goal has been to protect workers involved with the production of coal tar products. Although government standards are not for chrysene alone, they are useful in controlling exposure to total PAHs.

The National Institute for Occupational Safety and Health (NIOSH) has determined that workplace exposure to coal products can increase the risk of lung and skin cancer in workers and suggests a workplace exposure limit for coal tar products of 0.1 milligram of PAHs per cubic meter of air (0.1 $mg/m^3$) for a 10-hour workday, 40-hour workweek. NIOSH has not suggested a specific workplace limit for chrysene. The Occupational Safety and Health Administration (OSHA) has set a legal limit of 0.2 milligram of all PAHs per cubic meter of air (0.2 $mg/m^3$).

# 2. HEALTH EFFECTS SUMMARY

## 2.1 INTRODUCTION

This section summarizes and graphs data on the health effects concerning exposure to chrysene. The purpose of this section is to present levels of significant exposure for chrysene based on key toxicological studies, epidemiological investigations, and environmental exposure data. The information presented in this section is critically evaluated and discussed in Sect. 4, Toxicological Data, and Sect. 7, Potential for Human Exposure.

This Health Effects Summary section comprises two major parts. Levels of Significant Exposure (Sect. 2.2) presents brief narratives and graphics for key studies in a manner that provides public health officials, physicians, and other interested individuals and groups with (1) an overall perspective of the toxicology of chrysene and (2) a summarized depiction of significant exposure levels associated with various adverse health effects. This section also includes information on the levels of chrysene that have been monitored in human fluids and tissues and information about levels of chrysene found in environmental media and their association with human exposures.

The significance of the exposure levels shown on the graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of overt clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with frank effects (Frank Effect Level, FEL). Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (Lowest-Observed-Adverse-Effect Level, LOAEL) or exposure levels below which no adverse effects (No-Observed-Adverse-Effect Level, NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels) are of interest to health professionals and citizens alike.

Adequacy of Database (Sect. 2.3) highlights the availability of key studies on exposure to chrysene in the scientific literature and displays these data in three-dimensional graphs consistent with the format in Sect. 2.2. The purpose of this section is to suggest where there might be insufficient information to establish levels of significant human exposure. These areas will be considered by the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, and the National Toxicology Program (NTP) of the U.S. Public Health Service in order to develop a research agenda for chrysene.

## 2.2 LEVELS OF SIGNIFICANT EXPOSURE

### 2.2.1 Key Studies and Graphical Presentations

To help public health professionals address the needs of persons living or working near hazardous waste sites, the toxicology data summarized in this section are organized first by route of exposure (inhalation, ingestion, and dermal) and then by toxicological end points that are categorized into six general areas--lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, genetic toxicity, and carcinogenicity. The data are discussed in terms of three exposure periods--acute, intermediate, and chronic.

Two kinds of graphs are used to depict the data. The first type is a "thermometer" graph. It provides a graphical summary of the human and animal toxicological end points and levels of exposure for each exposure route for which data are available. The ordering of effects does not reflect the exposure duration or species of animal tested. The second kind of graph shows Levels of Significant Exposure (LSE) for each route and exposure duration. The points on the graph showing NOAELs and LOAELs reflect the actual doses (levels of exposure) used in the key studies. No adjustments for exposure duration or intermittent exposure protocol were made.

Adjustments reflecting the uncertainty of extrapolating animal data to man, intraspecies variations, and differences between experimental versus actual human exposure conditions were considered when estimates of levels posing minimal risk to human health were made for noncancer end points. These minimal risk levels were derived for the most sensitive noncancer end point for each exposure duration by applying uncertainty factors. These levels are shown on the graphs as a broken line starting from the actual dose (level of exposure) and ending with a concave-curved line at its terminus. Although methods have been established to derive these minimal risk levels (Barnes et al. 1987), shortcomings exist in the techniques that reduce the confidence in the projected estimates. Also shown on the graphs under the cancer en point are low level risks ($10^{-4}$ to $10^{-7}$) reported by EPA if available. In addition, the actual dose (level of exposure) associated with tumor incidence is plotted.

#### 2.2.1.1 Inhalation exposure

No information was found in the available literature concerning the effects of chrysene ollowing inhalation exposure.

**Lethality and decreased longevity.** No information is available.

**Systemic toxicity.** No information is available.

**Developmental toxicity.** No information is available.

**Reproductive toxicity.** No information is available.

**Genotoxicity.** No information is available.

**Carcinogenicity.** No reports directly correlating inhalation exposure to chrysene and cancer induction are available, although reports of cancer among individuals exposed to mixtures of PAHs

containing chrysene lend qualitative support to its potential for carcinogenicity in humans.

#### 2.2.1.2 Oral exposure

No information was found in the available literature concerning the effects of chrysene following oral exposure.

**Lethality and decreased longevity**. No information is available.

**Systemic toxicity**. No information is available.

**Developmental toxicity**. No information is available.

**Reproductive toxicity**. No information is available.

**Genotoxicity**. No information is available.

**Carcinogenicity**. No information is available.

#### 2.2.1.3 Dermal exposure

No information is available on the effects of chrysene following short-term dermal exposure. Chrysene has been shown to be carcinogenic following long-term dermal exposure. This conclusion is based on observations of laboratory animals since no data are available for human exposure; results are summarized in Figs. 2.1 and 2.2.

**Lethality and decreased longevity**. No information is available.

**Systemic toxicity**. No information is available.

**Developmental toxicity**. No information is available.

**Reproductive toxicity**. No information is available.

**Genotoxicity**. No information is available.

**Carcinogenicity**. No information directly correlating human dermal exposure to chrysene and cancer induction is available, although reports of skin tumors among individuals exposed to mixtures of PAHs containing chrysene lend some qualitative support to its potential for carcinogenicity in humans.

Studies in laboratory animals have demonstrated the ability of chrysene to induce skin tumors following long-term dermal exposure. Mice receiving doses of 1.2 mg/kg/day applied to their skin for 17 months developed benign and malignant skin tumors (Hecht et al. 1974). No estimate of human risk has been calculated.

### 2.2.2 Biological Monitoring

The available biological monitoring techniques can be useful in predicting whether exposure to chrysene or other PAHs has occurred, but they may not be useful in estimating body doses. Individual variability, confounding effects of drugs, and specificity of the techniques are likely to complicate the association between chrysene metabolites in the body and environmental exposure. The most common tests for determining exposure to PAHs in humans are examinations of tissues, blood, and urine

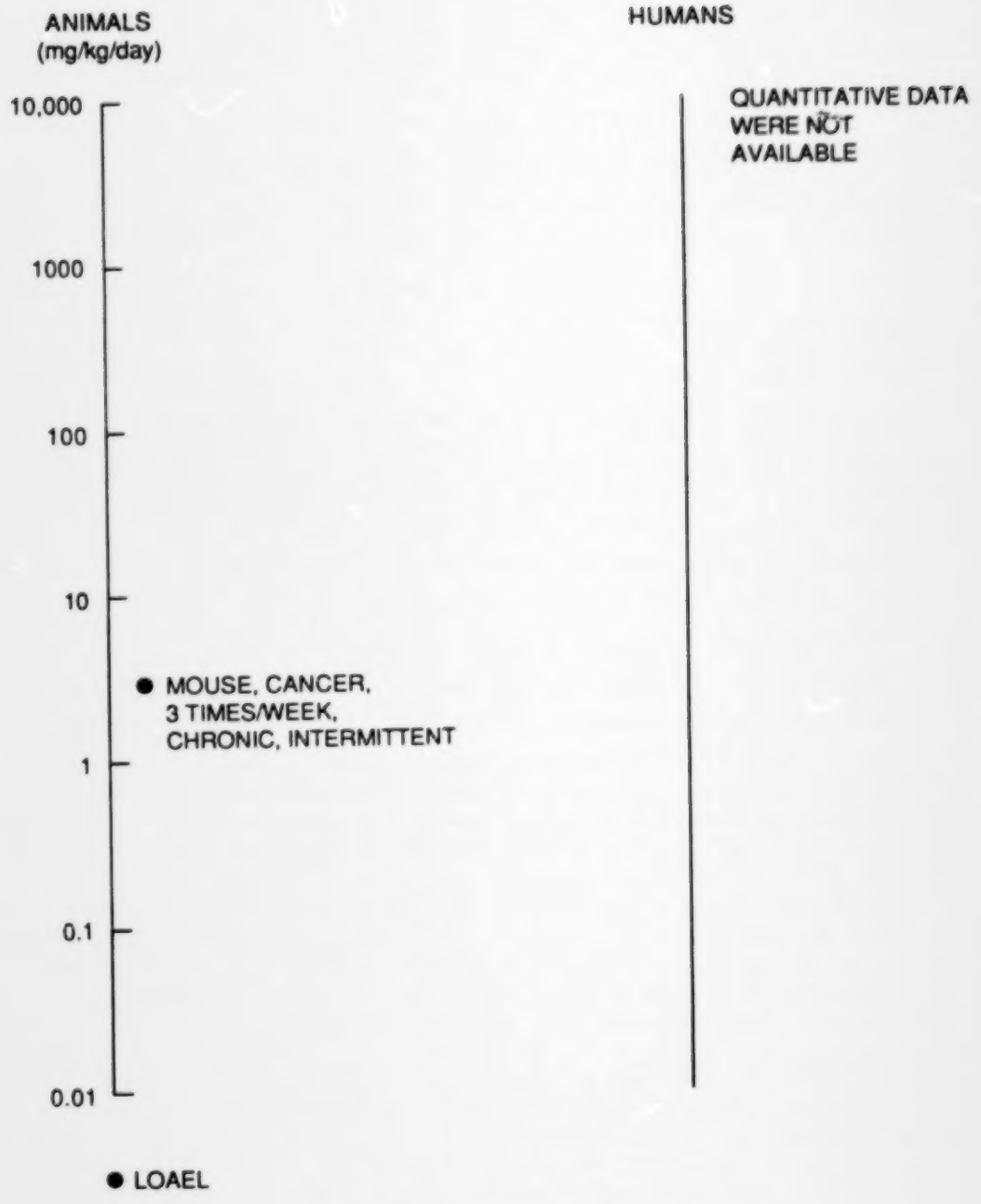



**Fig. 2.1. Effects of chrysene—dermal exposure.**

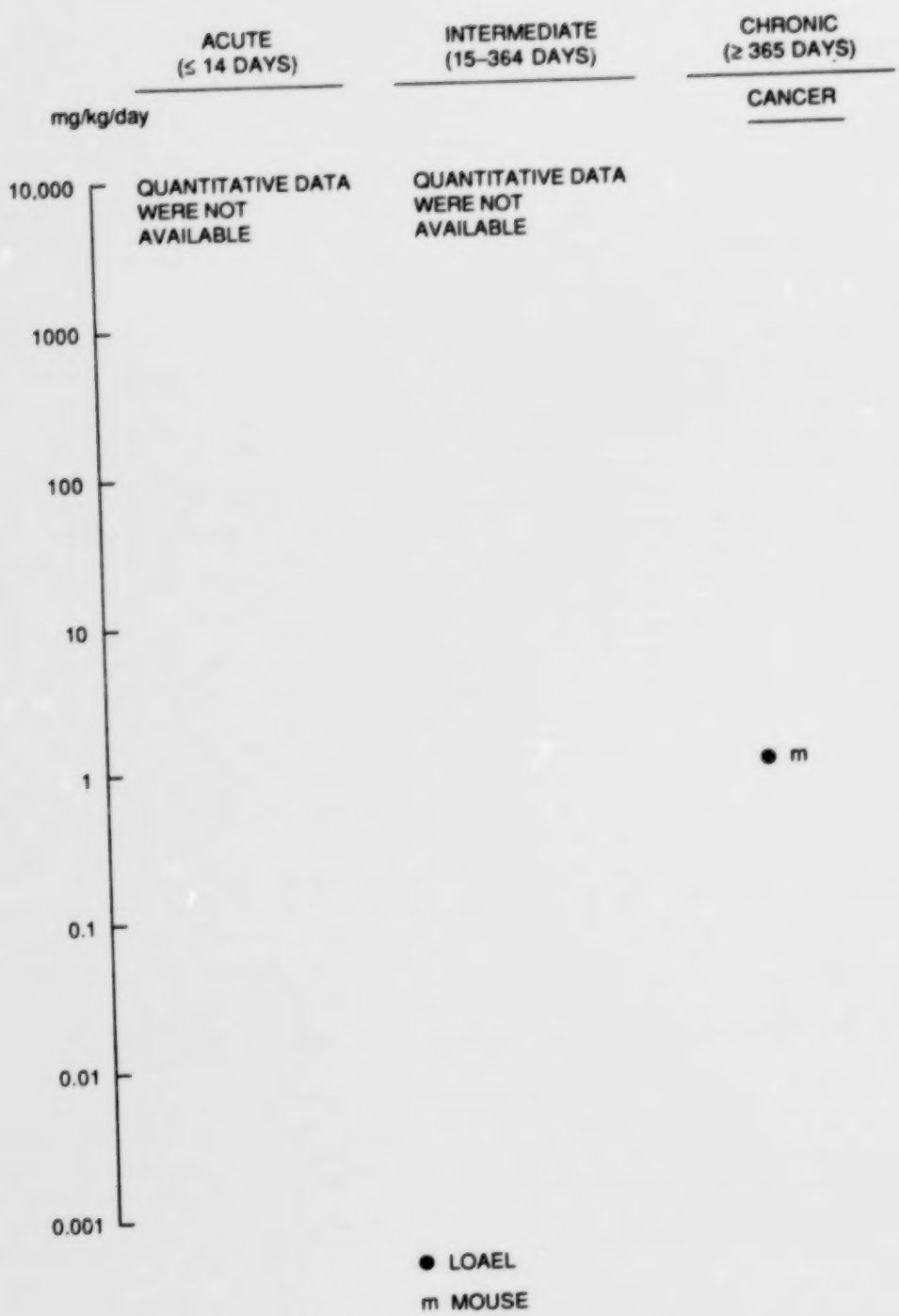



**Fig. 2.2. Levels of significant exposure for chrysene—dermal.**

for the presence of PAHs or PAH metabolites. Currently available biological monitoring techniques are discussed in detail in Sect. 8.

Modica et al. (1982) and Bartosek et al. (1984) used gas-liquid chromatography to determine the presence of PAHs in blood, mammary and adipose tissue, liver, and brain of rats. However, examples from examining human tissue samples using this method were not found in the available literature.

In the body, chrysene can be converted by specific cellular enzymes to a dihydrodiol and further metabolized to diol epoxides that can bind to DNA and form DNA adducts (Phillips et al. 1986). In vitro formation of diol epoxide adducts was quantified using high-performance liquid chromatography (Mushtaq et al. 1987). In the $^{32}P$ postlabeling technique, a tissue sample is taken from an exposed individual, and DNA from the exposed cells is digested and labeled with radioactive phosphorus ($^{32}P$). Thin-layer chromatography is then used to determine the presence of altered DNA, and scintillation counting is used to quantify the adducts (Randerath et al. 1985). Although the presence of chrysene diol epoxide-DNA adducts is directly associated with exposure to chrysene, this technique of analyzing adducts is limited in its usefulness to predict body dose from environmental exposure because interindividual differences in the rate or extent of the removal of the diol epoxide-DNA adducts could complicate the estimate of body dose. A technique has also been developed that tests for the presence of antibodies to the PAH diol epoxide-DNA adducts in blood using immunoassays (Harris 1985a,b; Harris et al. 1986). A patent application has been submitted for a method and kit for detecting antibodies in human sera to diol epoxide-DNA adducts by immunoassay (Harris 1985b). This method has been used to examine occupationally exposed individuals and smokers.

Chrysene has been detected in the urine of individuals occupationally exposed to atmospheric PAHs and in individuals treated with therapeutic coal tar for psoriasis (Becher and Bjorseth 1983, Becher et al. 1984, Clonfero et al. 1986).

A technique to detect benzo[a]pyrene using an antibody-based fiberoptics biosensor has been tested recently. This technique has been investigated using sample solutions containing benzo[a]pyrene and may be useful for assessing an individual's exposure to other PAHs, provided appropriate antibodies are used (Vo-Dinh et al. 1987).

### 2.2.3 Environmental Levels as Indicators of Exposure and Effects

#### 2.2.3.1 Levels found in the environment

Chrysene has been detected in air, water, and soils, but limited information is available to adequately characterize exposures in these media. Chrysene air concentrations in U.S. cities have been reported in the range of 0.04 and 4.8 ng/m$^3$ (Gordon and Bryan 1973, Fox and Staley 1976). Chrysene concentrations in finished drinking waters of the United States have been reported in the range of <1 to 8 ng/L (Sorrell et al. 1981). No data are available on chrysene levels in U.S. soil, but concentrations of total PAHs, including chrysene, have been reported in the range of 4 to 13 mg/kg in relatively rural areas of the United States (summarized by Blumer et al. 1977).

Chrysene may occur in the soil and on particulate matter in the air surrounding waste sites, such as former manufactured-gas plants and creosote wood treatment plants. However, exposure levels at these sites have not yet been published.

Data are not available that relate these levels to significant health effects in humans following environmental exposures.

#### 2.2.3.2 Human exposure potential

Humans may be exposed to chrysene in air, water, soil, and food, and each of these media constitutes a normal route of background exposures. Background exposures to chrysene are expected to occur at very low levels. Much higher exposure concentrations are associated with tobacco smoke and with some occupational environments. At hazardous waste sites, exposure concentrations may also be higher than background, and humans may be exposed to chrysene via contact with soil or inhalation of particulate matter in air. Estimates of body doses or tissue levels associated with chrysene intake require (1) information on the chemical concentrations in soil and air, (2) certain assumptions about factors controlling intake, and (3) information on absorption of chrysene from soil or particulate matter.

Information on the first two of these data needs is relatively site-specific in nature and cannot be generalized across all sites. Quantitative toxicological information on the absorption of chrysene and other PAHs from soil or particulate matter is lacking, although absorption is expected to be low (Becher et al. 1984). Consequently, estimates of doses following exposure to chrysene in soil or air are based on assumptions regarding dermal absorption of chrysene from soil and absorption of incidentally ingested chrysene on soil, or inhaled chrysene on particulate matter. These assumptions lend uncertainty to any risk assessment of the potential health effects of chrysene following environmental exposures.

## 2.3 ADEQUACY OF DATABASE

### 2.3.1 Introduction

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each of the 100 most significant hazardous substances found at facilities on the CERCLA National Priorities List. Each profile must include the following content:

"(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This section identifies gaps in current knowledge relevant to developing levels of significant exposure for chrysene. Such gaps are identified for certain health effect end points (lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, and carcinogenicity) reviewed in Sect. 2.2 of this profile in developing levels of significant exposure for chrysene and for other areas such as human biological monitoring and mechanisms of toxicity. The present section briefly summarizes the availability of existing human and animal data, identifies data gaps, and summarizes research in progress that may fill such gaps.

Specific research programs for obtaining data needed to develop levels of significant exposure for chrysene will be developed by ATSDR, NTP, and EPA in the future.

### 2.3.2 Health Effect End Points

#### 2.3.2.1 Introduction and graphic summary

The availability of data for health effects in humans and animals is depicted on bar graphs in Figs. 2.3 and 2.4, respectively.

The bars of full height indicate that there are data to meet at least one of the following criteria:

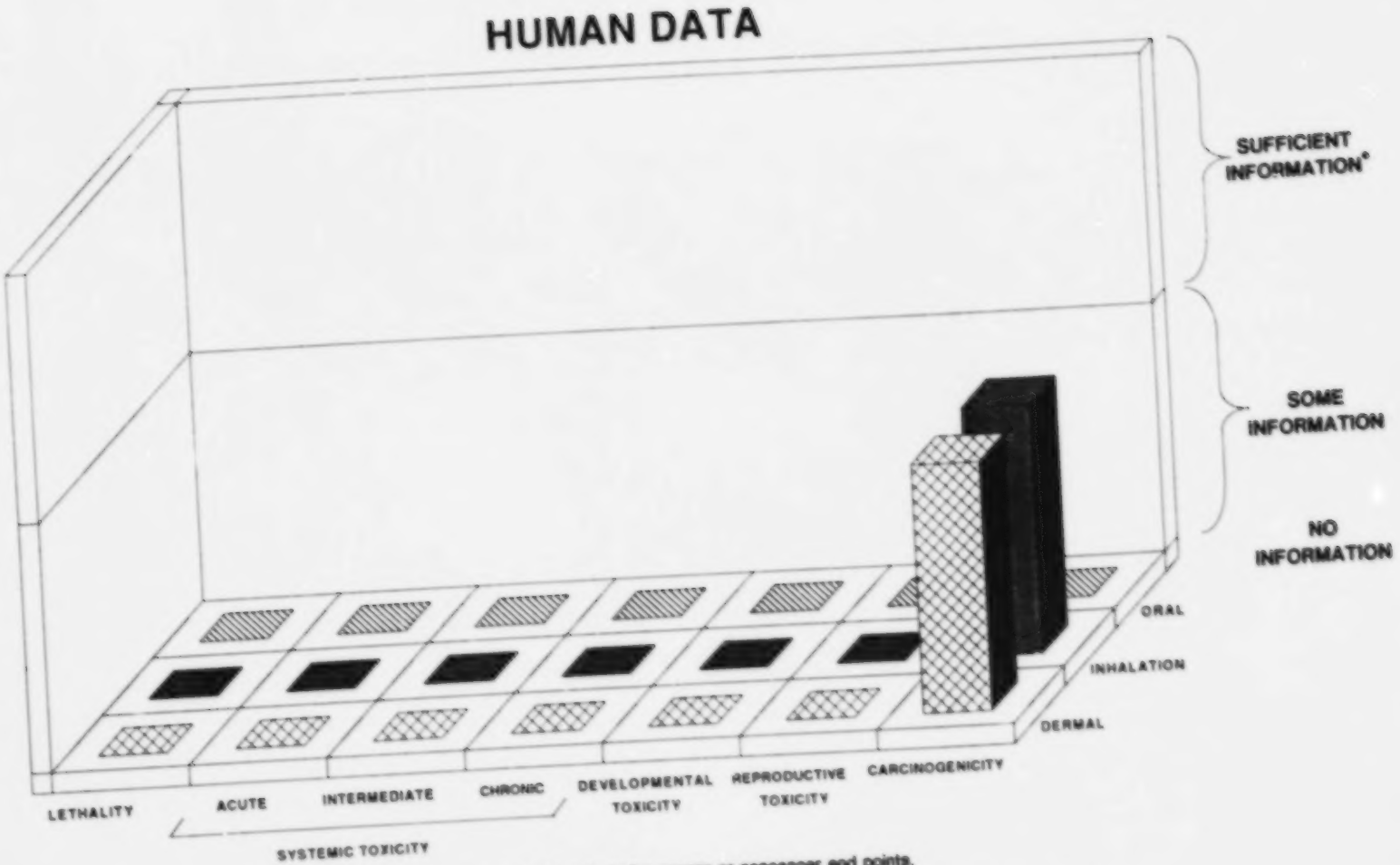
1. For noncancer health effect end points, one or more studies are available that meet current scientific standards and are sufficient to define a range of toxicity from no-effect levels (NOAELs) to levels that cause effects (LOAELs or FELs).
2. For human carcinogenicity, a substance is classified as either a "known human carcinogen" or "probable human carcinogen" by both EPA and the International Agency for Research on Cancer (IARC) (qualitative), and the data are sufficient to derive a cancer potency factor (quantitative).
3. For animal carcinogenicity, a substance causes a statistically significant number of tumors in at least one species, and the data are sufficient to derive a cancer potency factor.
4. There are studies which show that the chemical does not cause this health effect via this exposure route.

Bars of half height indicate that "some" information for the end point exists, but does not meet any of these criteria.

The absence of a column indicates that no information exists for that end point and route.

#### 2.3.2.2 Description of highlights of graphs

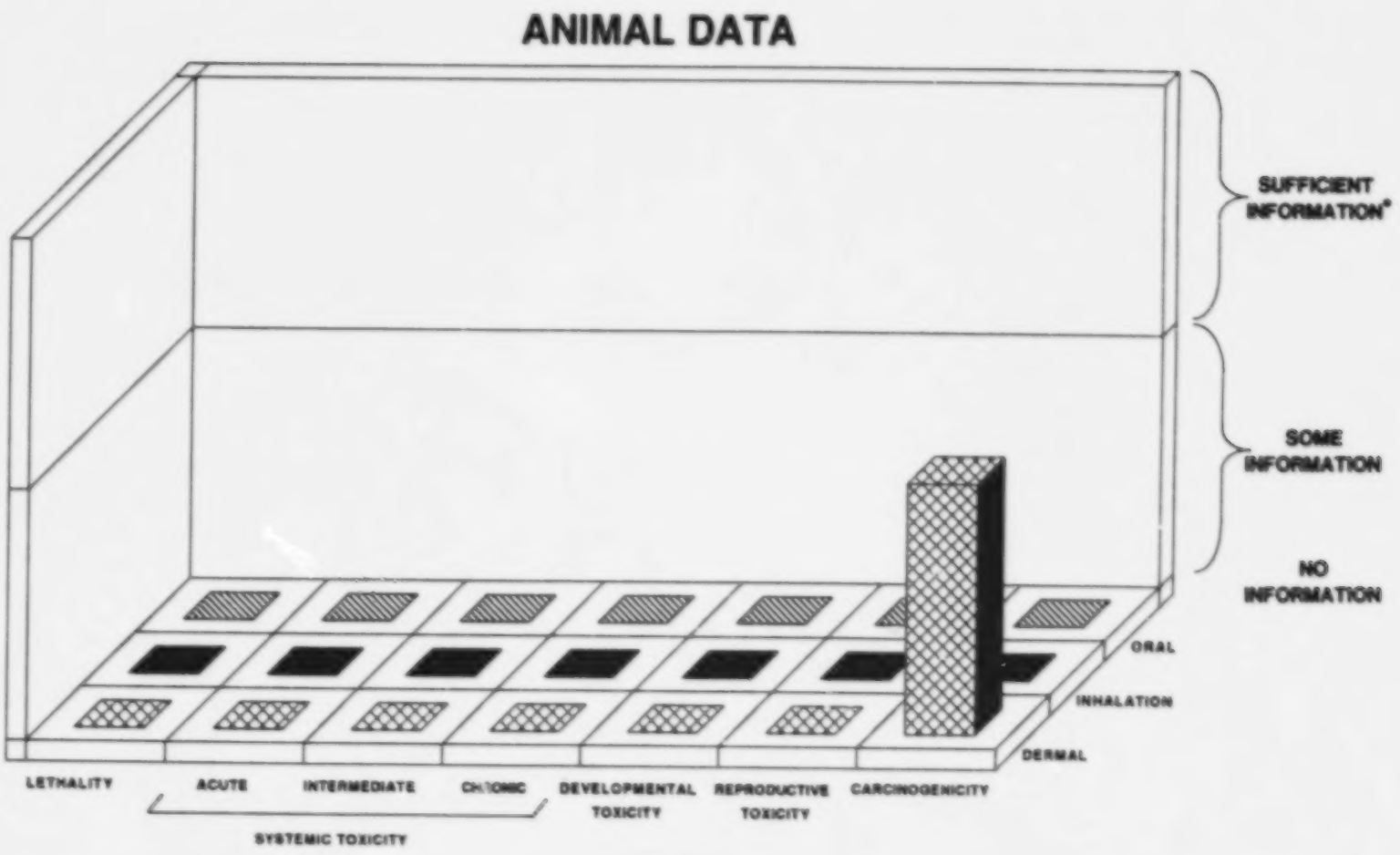
Figure 2.3 indicates that there are no data available to assess significant exposure levels of chrysene alone for humans. Reports of adverse health effects such as carcinogenicity by the inhalation and dermal routes of exposure do exist for mixtures of chemicals that




*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of chrysene by the inhalation and dermal routes of exposure has been assessed on the basis of human exposure to complex mixtures of chemicals containing this compound, not on the basis of the compound alone.

**Fig. 2.3. Availability of information on health effects of chrysene (human data).**




*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

**Fig. 2.4. Availability of information on health effects of chrysene (animal data).**

include chrysene, thus providing some information to qualitatively assess the role of chrysene as a carcinogen in humans.

As displayed in Fig. 2.4, some data are available to assess only the dermal carcinogenicity of chrysene in animals. No information could be found on the effects of chrysene following oral or inhalation exposure.

#### 2.3.2.3 Summary of relevant ongoing research

Research is ongoing in the areas of chrysene's molecular dosimetry, as well as into its biological mechanisms of action such as those of DNA binding and repair. A comparative potency method to quantitatively assess the carcinogenic risks for PAHs is under development by the Carcinogen Assessment Group, the Office of Solid Waste, the Office of Drinking Water, and the Office of Air Quality Planning and Standards of the EPA (EPA Contract No. 68-02-4403), and is being applied to the data available for chrysene.

### 2.3.3 Other Information Needed for Human Health Assessment

#### 2.3.3.1 Toxicokinetics and mechanisms of action

The metabolism of chrysene has been examined in cell cultures, human and rodent skin organ cultures, and microsomal preparations. The metabolism data collected suggest a mechanism of action similar to the one established for benzo[a]pyrene. There is limited information on the toxicokinetics of chrysene administered via the oral route. There is no information on the mechanistic aspects of the steps leading to excretion of chrysene. The information available on chrysene does not allow extrapolation from one route of exposure to another. No current studies were identified as being likely to provide this information.

#### 2.3.3.2 Adequacy of data on biological monitoring

The biological monitoring techniques in which DNA adducts are quantified are limited because inborn factors, environmental chemistry, and drugs can alter the activity of the enzymes responsible for converting chrysene to the diol epoxides that bind to DNA. There is a lack of information concerning the use of these techniques in occupationally or environmentally exposed individuals. Additional research should include further investigation of the formation of adducts following these exposure situations.

The technique that uses immunoassays to determine the presence of antibodies to adducts in blood has been tested in occupationally exposed humans and smokers (Harris 1985b, Harris et al. 1986). This technique has shown a direct association between sera positive for antibodies and occupational exposure or smoking. The reliability of this method needs to be examined further in other nonoccupational exposure situations.

The presence of PAHs in urine is an indication that exposure has occurred. However, in occupational studies, the amount of PAH concentration in the urine did not adequately reflect environmental PAH concentrations (Becher and Bjorseth 1983, Becher et al. 1984). This discrepancy was reported to result from the nonbioavailability of

particle-bound chrysene; therefore, this method should be further examined for its applicability in other exposure situations.

In addition, smoking cigarettes and some occupationally related activities result in human exposure to PAHs; therefore, the determination of biological levels of PAHs in smokers and in the general population must be examined more fully to properly assess environmental exposure.

#### 2.3.3.3 Environmental considerations

The accuracy and precision of the analytical methods used to measure ambient chrysene are somewhat limited. But the current methods, if properly conducted, are sufficient to record ambient levels of chrysene; however, some methods have limited sensitivity.

Limited data are available to characterize background levels of chrysene, or levels typically found at hazardous waste sites. Comprehensive monitoring studies are being conducted at or around many hazardous waste sites, but the data are not yet available in a single database.

No quantitative data are available on the bioavailability of chrysene in soil or sorbed onto particulate matter in air. This lack of information limits our understanding of potential health risks in humans following exposure to these media.

Information on the fate of chrysene sorbed onto particulate matter in air is presently unclear. The role of photochemical oxidation in the removal or activation of chrysene in air needs to be elucidated. Also, additional information on biodegradation processes and rates in aquatic and terrestrial systems is needed.

Only limited information is available on the interactions of chrysene in vivo and with other chemicals typically found in the environment and at hazardous waste sites. Consequently, risks associated with exposure to chrysene in the environment are not completely understood.

# 3. CHEMICAL AND PHYSICAL INFORMATION

## 3.1 CHEMICAL IDENTITY

The chemical formula, structure, synonyms, and identification numbers for chrysene are listed in Table 3.1.

## 3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of chrysene are given in Table 3.2.

**Table 3.1. Chemical identity of chrysene**

Chemical name: chrysene

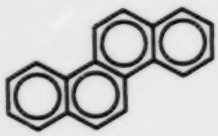
Synonyms: 1,2-benzo[a]phenanthrene; benzo[a]phenanthrene; 1,2-benzphenanthrene; benz[a]phenanthrene; 1,2,5,6-dibenzonapthalene (IARC 1983)[a]

Trade name: not applicable

Chemical formula: $C_{18}H_{12}$ (IARC 1983)

Wiswesser line notation: L E6 B666J (HSDB 1987)

Chemical structure:



Identification numbers:

CAS Registry No.: 218-01-9
NIOSH RTECS No: GC0700000
EPA hazardous waste No.: U050
OHM-TADS No.: not available
DOT/UN/NA/IMCO shipping No.: not available
STCC No.: not available
Hazardous Substances Data Bank No.: 2810
National Cancer Institute No.: not available

[a]Confusion exists in the literature concerning the naming of this compound, mainly due to the fact that two different systems (Richter and IUPAC) of numbering ring structures have been used; the IARC reference does not acknowledge that this confusion exists and that some of the synonyms listed are incorrect with regard to nomenclature.

**Table 3.2. Physical and chemical properties of chrysene**

| Property | Value | Reference |
|---|---|---|
| Molecular weight | 228.3 g/mol | IARC 1983 |
| Color | Colorless with red blue fluorescence | CRC 1987 |
| Physical state | Rhombic plates (recrystallized from benzene/acetic acid) | CRC 1987 |
| Odor | Unknown | |
| Melting point | 255–256°C | CRC 1987 |
| Boiling point | 448°C; sublimes in vacuo | CRC 1987, Merck Index 1983 |
| Autoignition temperature | Unknown | |
| Solubility | | |
| Water | 1.5–2.2 μg/L | IARC 1983 |
| Organic solvents | Slightly soluble in acetone, carbon disulfide, diethyl ether, ethanol, glacial acetic acid, toluene, and hot xylene. Soluble in benzene | IARC 1983 |
| Biological fluids | Unknown | |
| Density | 1.274 | CRC 1987 |
| Partition coefficients | | |
| Octanol-water ($K_{ow}$) | $4.1 \times 10^5$ | EPA 1982 |
| Soil-organic carbon-water ($K_{oc}$) | $2 \times 10^5$ | EPA 1982 |
| Vapor pressure (20°C) | $6.3 \times 10^{-9}$ mm Hg | EPA 1982 |
| Henry's Law constant | $1.05 \times 10^{-6}$ | EPA 1982 |
| Flashpoint | Unknown | |
| Flammability limits | Unknown | |
| Conversion factor[a] | 1 ppm = 9.34 mg/m$^3$ | Verschueren 1983 |

[a]Calculated using the ideal gas law, PV = nRT at 25°C.

# 4. TOXICOLOGICAL DATA

## 4.1 OVERVIEW

Chrysene is absorbed by the oral route of exposure. Absorption may also occur following dermal exposure. Data are not available to determine whether chrysene is absorbed via the lungs. Absorbed chrysene is distributed to several tissues; in fact, it was found in all five tissues studied by Modica et al. (1983). Modica also found that chrysene accumulates preferentially in the adipose and mammary tissues. It is metabolized to conjugated derivatives and eliminated. Orally administered chrysene was predominantly eliminated via the feces.

Chrysene is metabolized to reactive derivatives, presumably bay-region diol epoxides, that are believed to be responsible for its carcinogenic (as well as mutagenic) activity in experimental systems. Compared with benzo[a]pyrene, chrysene is a weak carcinogen by the dermal route of exposure. Its carcinogenicity has not been studied by other routes. Mutation is thought to be a necessary (albeit insufficient) step for chrysene's carcinogenic activity. It is a weak mutagen in experimental systems.

There is no information on other toxic effects of chrysene in humans and laboratory animals following inhalation, oral, and dermal exposures. Carcinogenic PAHs as a group cause skin disorders and have an immunosuppressive effect. However, subcutaneous injection of chrysene in female B6C3F$_1$ mice did not significantly suppress the antibody-forming cell response compared to corn oil vehicle controls (White et al. 1985). The LD50 for chrysene administered intraperitoneally was found to be >320 mg/kg body weight in mice (Simmon et al. 1979).

## 4.2 TOXICOKINETICS

### 4.2.1 Overview

Chrysene is absorbed by the oral route. Absorption may also occur following dermal exposure. No direct evidence is available for absorption of chrysene via the lungs. Absorbed chrysene is distributed to several tissues. The relative rate of uptake is dependent on the blood perfusion rate of the tissue. Chrysene accumulates preferentially in the adipose and mammary tissues. Chrysene undergoes metabolic transformation in humans and animals to reactive intermediates responsible for its toxicity. The major metabolic products isolated include trans-dihydrodiols, phenols, and bay-region diol epoxides and triol epoxides. Chrysene-1,2-diol-3,4-epoxide and 9-hydroxychrysene-1,2-diol-3,4-epoxide have been shown to react covalently with DNA. Metabolism of chrysene to 9-hydroxychrysene 1,2-diol-3,4-epoxide has been demonstrated in mouse skin but not human skin.

After oral dosing, most of the chrysene is eliminated and recovered in the feces. However, it is not known how much of the orally dosed chrysene is absorbed and excreted in the feces. By analogy to other PAHs, the excreted material is expected to consist of unchanged hydrocarbon and polar metabolites, for example, sulfates, glucuronides, and glutathione conjugates.

### 4.2.2. Absorption

#### 4.2.2.1 Inhalation

**Human.** No quantitative information on the absorption of chrysene via the respiratory tract was found. Absorption of chrysene via this route is inferred from identification of chrysene and its metabolites in individuals exposed to PAHs in an industrial environment containing high levels of PAH in the atmosphere (Becher and Bjorseth 1983). Chrysene was also identified in the urine of cigarette smokers (Becher 1986).

**Animal.** No information was found on the absorption of chrysene via the respiratory tract. By analogy to benzo[a]pyrene, pulmonary absorption of chrysene is expected to be efficient and subject to similar controlling factors. Specifically, the role of metabolism in absorption mechanisms, particle size, and mucociliary clearance is anticipated to influence the rate of absorption via the respiratory tract (Kao et al. 1985, Sanders et al. 1986, Creasia et al. 1976, Tornquist et al. 1985, Medinsky and Kampcik 1985).

#### 4.2.2.2 Oral

**Human.** No data on the absorption of chrysene via the gastrointestinal tract in humans were identified.

**Animal.** Oral absorption of chrysene administered in the diet (Chang 1943) or by gavage (Chang 1943, Modica et al. 1983) has been studied in the rat. Chrysene was absorbed via the gastrointestinal tract. Recoveries of the hydrocarbon and its metabolites in the feces ranged from 25 to 41% of the administered doses (11.4 mg/rat/2 mL olive oil and 11.4 mg/rat/1 mL olive oil, respectively) in 72 h. The extent of fecal excretion of chrysene was dependent upon the dose and concentration of chrysene and the vehicle used for administration (Modica et al. 1983). Chang (1943) reported higher excretion of hydrocarbons (an average of 79%) in the feces following dietary (250 mg/rat) and gavage (100 mg/rat) administration. Based on the available literature, it is not possible to quantify the portion of the absorbed chrysene excreted and recovered in the feces.

#### 4.2.2.3 Dermal

**Human.** No specific data on the dermal absorption of chrysene in humans was identified. The dermal absorption rate of chrysene, however, may be anticipated to be similar to that of benzo[a]pyrene (Kao et al. 1985) in view of the comparatively efficient metabolism reported for chrysene in human skin (Weston et al. 1985). It has also been reported that cutaneously applied therapeutical coal tar containing PAHs, including chrysene, is correlated with a rise in PAH levels in the

urine, suggesting that chrysene, like benz[a]anthracene and benzo[a]pyrene, is absorbed through the skin (Clonfero et al. 1986).

**Animal.** No quantitative data on the dermal absorption of chrysene in animals were identified. Chrysene is metabolized in mouse skin at relatively high rates (Hodgson et al. 1983, Weston et al. 1985) that should facilitate dermal uptake, as demonstrated with benzo[a]pyrene (Kao et al. 1985, Sanders et al. 1986). Short-term organ cultures using mouse skin taken from the shaved backs of mice demonstrated that induction of cutaneous drug-metabolizing enzymes can result in a two- to threefold increase in the in vitro permeation of topical [$^{14}$C]-B[a]P.

### 4.2.3 Distribution

There is no information on the distribution of either inhaled or dermally absorbed chrysene.

Orally absorbed chrysene is distributed to several tissues in the rat (Modica et al. 1983, Bartosek et al. 1984). Peak-level concentrations in blood and liver were reached 1 h after oral administration. Tissue levels in the liver were 4 to 10 times higher than blood levels. Maximum concentration in adipose tissue was reached in ~3 h (Bartosek et al. 1984). The relative tissue affinity after 24 h was determined as: adipose > mammary > brain > liver > blood. The tissue accumulation was not dose-dependent (except for mammary tissue), suggesting saturation of the absorption mechanism (Modica et al. 1983).

### 4.2.4 Metabolism

The metabolism of chrysene in human and animal systems proceeds via the biotransformation pathways established for benzo[a]pyrene (Cooper et al. 1983, Levin et al. 1982, Sims 1982, Thakker et al. 1985) (see Fig. 4.1).

The metabolism of chrysene in rat liver microsomes (MacNicoll et al. 1979) produces the 1,2-, 3,4-, and 5,6-dihydrodiols. Similar results have been reported following incubation of chrysene in human skin culture (Weston et al. 1985) and mouse skin (Weston et al. 1985, Hodgson et al. 1983). The phenolic metabolites of 1-hydroxy-, 3-hydroxy-, and 4-hydroxychrysene have also been isolated from rat liver preparations (Jacob et al. 1987). No arene oxide intermediates of chrysene have been isolated, although the formation of dihydrodiols (Sims and Grover 1974, Sims and Grover 1981) and phenols provides evidence of their presence in incubation mixtures. The 1,2-dihydrodiol is metabolized to the bay-region diol epoxide, chrysene 1,2-diol-3,4-epoxide, in mouse and human skin (Weston et al. 1985, Hodgson et al. 1986) and in hamster cells (Phillips et al. 1986). The formation of a triol epoxide metabolite of chrysene, 9-hydroxychrysene 1,2-diol-3,4-epoxide, has been reported in mouse skin (Weston et al. 1985, Hodgson et al. 1983), hamster cells (Phillips et al. 1986), and rat liver microsomal preparations (Hodgson et al. 1985, Nordquist et al. 1981). Metabolism of chrysene to 9-hydroxychrysene 1,2-diol-3,4-oxide has not been demonstrated in human skin (Weston et al 1985). Both intermediates, chrysene 1,2-diol-3,4-epoxide and 9-hydroxychrysene 1,2-diol-3,4-epoxide, possess alkylating activity, as evidenced by isolation of covalent adducts with DNA from

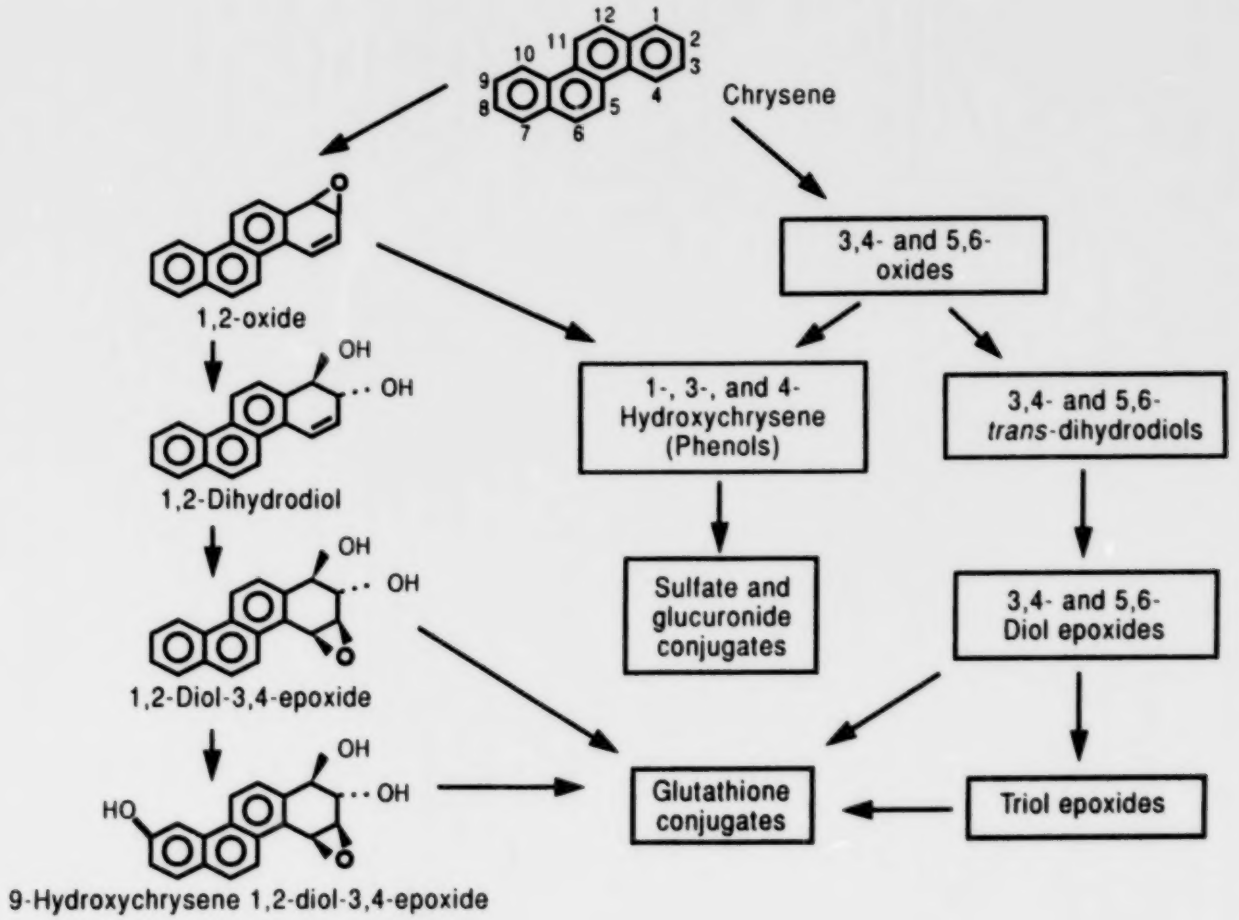



**Fig. 4.1. Metabolic fate of chrysene.**

mouse skin. This finding is consistent with the proposed bay-region theory of PAH carcinogenesis (Levin et al. 1982, Thakker et al. 1985).

Other biological transformations reported for chrysene involve conjugation of bay-region diol-epoxide and triol-epoxide metabolites with glutathione (Hodgson et al. 1986, Robertson and Jernstrour 1986) and the formation of sulfate and glucuronide conjugates of phenols and *trans*-dihydrodiols (Sims and Grover 1974, Sims and Grover 1981).

### 4.2.5 Excretion

The steps involved in the excretion of chrysene are likely to be those established for other PAHs. Metabolism, hepatobiliary excretion, and elimination through feces are the dominant features in this process that have been reported for the other PAHs (Schlede et al. 1970). The material excreted is expected to consist predominantly of dihydrodiol and phenol conjugates (glucuronide and sulfate esters) and glutathione conjugates.

As the percentage of chrysene fed to rats in the diet increased from 0.2 to 1.0%, the percentage of excreted hydrocarbon also increased (Chang 1943). Chrysene was also found by Chang (1943) to be eliminated by the rat predominantly in the feces (average of 79% of administered dose); elimination was complete in ~2 days. Based on the available literature, it is not possible to quantify the contribution of unabsorbed chrysene in the excreted material.

## 4.3 TOXICITY

### 4.3.1 Lethality/Decreased Longevity

Pertinent data regarding lethality and decreased longevity in humans or experimental animals following inhalation, oral, and dermal exposure to chrysene could not be located in the available literature. The LD50 for chrysene administered intraperitoneally was found to be >320 mg/kg body weight in mice (Simmon et al. 1979).

### 4.3.2 Systemic/Target Organ Toxicity

No information is available on the systemic effects of chrysene in humans or experimental animals following inhalation, oral, and dermal exposures. The carcinogenic PAHs as a group cause skin disorders and have an immunosuppressive effect; however, specific results with chrysene have not been reported. Subcutaneous injection of chrysene in female B6C3F1 mice did not significantly suppress the antibody-forming cell response compared to the corn oil vehicle controls (White et al. 1985).

### 4.3.3 Reproductive and Developmental Toxicity

Pertinent data regarding the reproductive and developmental toxicity of chrysene in humans or experimental animals following inhalation, oral, and dermal exposure could not be located in the available literature. Perinatal administration of chrysene to mice by subcutaneous or intraperitoneal injection increased the incidence of liver tumors (Grover et al. 1975, Buening et al. 1979).

### 4.3.4 Genotoxicity of Chrysene

#### 4.3.4.1 Overview

The genetic toxicity of chrysene has been evaluated experimentally in short-term genetic toxicology assays utilizing prokaryotes and eukaryotes as target organisms for potential genotoxic and mutagenic effects. Metabolism of chrysene is essential to produce the observed positive effects in both in vivo and in vitro test systems. The test systems used to evaluate chrysene's genotoxicity and the results of each are summarized in Tables 4.1 and 4.2.

The genotoxicity of chrysene is dependent on metabolic activation, either exogenously supplied or endogenously present, and the balance between activation and detoxification pathways. The 1,2-diol-3-4-epoxide has been reported to be one of several metabolites of chrysene formed following incubation with rat-liver preparations (Nordquist et al. 1981). Studies have indicated that this diol-epoxide exhibits mutagenic activity in bacterial and mammaliam cell systems (Wood et al. 1977, 1979, 1982). Several other possible metabolites of chrysene have also been tested and shown to induce mutations in these cell systems (Wood et al. 1982, Glatt et al. 1986). These reactive metabolites interact with the DNA to form nucleic acid adducts (Hodgson et al. 1982, Vigny et al. 1982) that are generally regarded as an important determinant in mutagenesis and clastogenesis (Brendel and Ruhland 1984).

#### 4.3.4.2 General discussion.

The genotoxicity of chrysene is supported by positive results in both reverse and forward bacterial mutation studies, one human epithelial mutation study, one SHE cell transformation study, and two in vivo cytogenetic studies. Chrysene is not genotoxic in all test systems. Generally, the results with chrysene have been either weakly positive or negative.

Chrysene has been tested in vivo for two cytogenetic end points in germ cells and somatic cells of rodents. Weak induction of sister chromatid exchange and no induction of chromosomal aberrations in bone marrow cells were observed in Chinese hamsters exposed to chrysene via injection (Roszinsky-Kocher et al. 1979). In other studies, chromosomal aberrations were not induced in Chinese hamster bone marrow cells or spermatogonia in vivo, but a weak induction of aberrations was observed in mouse oocytes (Basler et al. 1977, Basler and Rohrborn 1978). Although no heritable gene mutation studies were available, the positive result reported for mouse oocytes may indicate the potential for heritable genetic effects.

Generally, negative findings were reported in in vitro test systems, for example, assays with most *Salmonella typhimurium* strains, *E. coli* strains, V79 cells, mouse prostate cells, and rat hepatocytes. Only one recent study reported positive mutagenic activity with chrysene in a human carcinoma cell line (Huberman et al. 1984). Negative results were reported for the host-mediated *Salmonella typhimurium* mutation assay (Simmon et al. 1979).

**Table 4.1. Genetic toxicity of chrysene (in vitro)**

| End points | Species (test systems) | Results[a] | References |
|---|---|---|---|
| DNA damage | *Escherichia coli* K12PQ37 (SOS repair) | Positive - activation | Ohta et al. 1984 |
| | *Escherichia coli* (pol A+/pol A−) | Negative - activation<br>Negative - no activation | Rosenkranz and Poirier 1979, McCoy et al. 1979 |
| DNA damage (UDS) | Primary rat hepatocytes | Negative - no activation | Tong et al. 1981 |
| Gene mutations | *Salmonella typhimurium* (his+/his−):TA100 | Positive - activation | Guthrie et al. 1982, McCann et al. 1975, Sakai et al. 1985, Wood et al. 1977 |
| | *Salmonella typhimurium* (his+/his−):TA97, TA98 | Positive - activation | Sakai et al. 1985 |
| | *Salmonella typhimurium* (his+/his−):TA1535, TA1536, TA1537, TA1538, TA1530 | Negative - activation | Rosenkranz and Poirier 1979, Simmon 1979a, Simmon et al. 1979 |
| | *Salmonella typhimurium* (his+/his−):TA1538 | Negative - activation (host-mediated) | Simmon et al. 1979 |
| | *Salmonella typhimurium* (8AGs/8AGr):TM677 | Positive - activation | Kaden et al. 1979 |
| | *Saccharomyces cerrevisiae* D3 (mitotic recombination) | Negative - activation | Simmon 1979b |
| | Chinese hamster V79 cells/HGPRT | Negative - activation | Huberman and Sachs 1976, Glatt et al. 1986 |
| | V79/Na+, K + ATPase | Negative - activation | Huberman and Sachs 1976 |
| | Human EUE epithelial-like cells (diptheria toxin resistance) | Negative - activation | Rocchi et al. 1980 |
| | Human epithelial teratoma cells/HGPRT | Positive - activation | Huberman et al. 1984 |
| Cell transformation | Syrian hamster embryo cells (clonal assay) | Positive - no activation | Pienta et al. 1977 |
| | Syrian hamster embryo cells | Negative - no activation | Huberman et al. 1972 |
| | Mouse prostate C3HG23 cells | Negative - no activation | Marquardt et al. 1972 |
| | Mouse prostate C3HM2 cells | Negative - no activation | Glatt et al. 1986 |

[a]The results reported in Tables 4.1 and 4.2 are based on activity profiles prepared by Waters et al. 1987, Gene-Tox files provided by J. S. Wassom, and/or personal review of the original citations.

**Table 4.2. Genetic toxicity of chrysene (in vivo)**

| End points | Species (test systems) | Results[a] | References |
|---|---|---|---|
| Sister chromatid exchange | Chinese hamster bone marrow cells | Positive | Roszinsky-Kocher et al. 1979 |
| Chromosomal aberrations | Chinese hamster bone marrow cells | Negative | Roszinsky-Kocher et al. 1979, Basler et al. 1977, Basler and Rohrborn 1978 |
| | Chinese hamster spermatogonia | Negative | Basler et al. 1977 |
| | NMRI mice oocytes | Positive | Basler et al. 1977, Basler and Rohrborn 1978 |

[a]The results reported in Tables 4.1 and 4.2 are based on activity profiles prepared by Waters et al. 1987, Gene-Tox files provided by J. S. Wassom, and/or personal review of the original citations.

The evidence for the genotoxicity of chrysene is equivocal. Although chrysene has tested negative in many test systems, there are also important positive results. Compared with other PAHs, especially B[a]P, chrysene shows weak genotoxic activity. In addition, the purity of the tested chrysene may have had an effect on the experimental results, because commercial chrysene contains other potentially genotoxic components (IARC 1983).

### 4.3.5 Carcinogenicity

#### 4.3.5.1 Overview

The carcinogenicity of chrysene has not been adequately studied. There are no reports directly correlating human chrysene exposure and tumor development, although humans are likely to be exposed by all routes. However, there are a number of reports associating human cancer and exposure to mixtures of PAHs that include chrysene. There is experimental evidence that chrysene is a skin carcinogen in animals following long-term dermal application. It is possible that chrysene could cause cancer in humans as well.

#### 4.3.5.2 Inhalation

**Human.** No studies on the carcinogenicity of chrysene in humans following inhalation exposure were found in the open literature. However, epidemiologic studies have shown an increased incidence of lung cancer in humans exposed to coke-oven emissions (Lloyd 1971, Redmond et al. 1972, Mazumdar et al. 1975), roofing-tar emissions (Hammond et al. 1976), and cigarette smoke (Wynder and Hoffmann 1967, Maclure and MacMahon 1980, Schottenfeld and Fraumeni 1982). Each of these mixtures contains chrysene as well as other carcinogenic PAHs and other potentially carcinogenic chemicals such as nitrosamines. It is thus impossible to evaluate the contribution of chrysene to the total human carcinogenicity of these mixtures because of their complexity and the presence of other carcinogens. Nonetheless, reports of this nature provide a qualitative suggestion of the potential for chrysene-induced carcinogenicity.

**Animal.** No studies on the carcinogenicity of chrysene in animals following inhalation exposure were found in the available literature.

#### 4.3.5.3 Oral

**Human.** No studies on the carcinogenicity of chrysene in humans following oral exposure were found in the available literature.

**Animal.** No studies on the carcinogenicity of chrysene in animals following oral exposure were found in the available literature.

#### 4.3.5.4 Dermal

**Human.** No studies on the carcinogenicity of chrysene in humans following dermal exposure were found in the available literature. As with inhalation exposure, however, there are reports of skin cancer among individuals exposed dermally to mixtures of PAHs containing chrysene. The earliest of these is the report of Pott (1775) of scrotal

cancer among chimney sweeps. More recently, skin cancer among those exposed dermally to shale oils has been reported (Purde and Etlin 1980). However, these reports provide only qualitative suggestions pertaining to the human/carcinogenic potential of chrysene because of the presence of other putative carcinogens in the mixtures.

**Animal.** Chrysene has been shown to cause skin tumors in mice following dermal application. Many of the earlier studies used samples of chrysene that were contaminated with methyl chrysenes and other potentially carcinogenic materials (IARC 1983). The results of a key study by Wynder and Hoffmann (1959) are shown in Table 4.3. As part of a study of the carcinogenicity of tobacco and its constituents, these authors tested several PAHs, including chrysene, as carcinogens on mouse skin. A group of 20 female Swiss mice received a concentration of 1% chrysene dissolved in acetone three times a week applied to their backs with a brush throughout their lifetimes. Elevated incidences of both papillomas and carcinomas were observed. No solvent control group was reported; however, since no papillomas or carcinomas were obtained for several of the PAHs tested, a solvent control group would most likely have been negative as well. Since only one dose level was employed, no dose-response information can be inferred from this study. It is likely that the chrysene used was contaminated with other carcinogens.

In another study, Horton and Christian (1974) applied 50 mg (60 µL) of a solution of 0.15% chrysene in decalin or *n*-dodecane/decalin (50/50) to the skin of 20 male C3H mice twice weekly for 82 weeks. The results of this study are also shown in Table 4.3. No solvent control was included; however, decalin and *n*-dodecane have been shown in other experiments to be noncarcinogenic in mice (Bingham and Falk 1969). Administration of *n*-dodecane/decalin led to a significant increase in the carcinogenic potency of chrysene compared with that obtained using decalin alone. Adequate mechanistic data with which to evaluate the nature of this cocarcinogenic activity are not available. Again, since only one dose level was employed in this experiment, no dose-response information can be inferred.

Hecht et al. (1974) synthesized highly purified chrysene (>99.9%) and applied it to the shaved backs of 20 female Swiss mice (Ha/ICR/Mil) three times weekly for 17 months. Each dose contained 100 µg chrysene in 0.1 mL acetone. As indicated in Table 4.3, both papillomas and carcinomas were observed. Although the authors state that a solvent control group was included, no results were reported; however, the lack of dermal carcinogenicity of acetone has been well established. The dose used is the lowest dose of chrysene that has been found to elicit malignant tumors in laboratory animals, and is approximately equal to an average dose of 1.2 mg/kg/day.

There are many reports of chrysene's ability to act as a tumor initiator in classic initiation/promotion bioassays on mouse skin using croton oil or phorbol myristate acetate as promoting agents (Van Duuren et al. 1966, Hecht et al. 1974, Levin et al. 1978, Wood et al. 1979, Wood et al. 1980). The difficulty inherent in extrapolating such experiments to human exposure precludes their being used as the basis for significant human exposure level development, although since

**Table 4.3. Carcinogenic activity of chrysene on mouse skin**

| Source | Dose (percent concentration) | Dose (mg/kg/day) | Number with tumors/ effective number (%)[a] | |
|---|---|---|---|---|
| | | | Papillomas | Carcinomas |
| Wynder and Hoffmann 1959[b] | 1.0 | 12 | 9/10 (90) | 8/10 (80) |
| Horton and Christian 1974[c] | 0.15 (decalin) | 1.8 | 1/12 (8) | 0/12 (0) |
| | 0.15 (*n*-dodecane/ decalin) | 1.8[d] | 5/19 (26) | 12/19 (63) |
| | | 1.8[e] | 2/17 (12) | 13/17 (76) |
| Hecht et al. 1974[f] | 0 | 0 | | |
| | 0.1 | 1.2 | 4/18 (22) | 4/18 (22) |

[a]Numbers within parentheses indicate percentages.

[b]Chrysene was applied with a brush to the backs of female Swiss mice as a solution in acetone three times weekly throughout their lifetimes.

[c]Chrysene was applied to the backs of male C3H mice as a solution in either decalin or *n*-dodecane/decalin (50/50) twice weekly for 82 weeks.

[d]Purified by authors.

[e]Commercial; used as received.

[f]Chrysene was applied to the backs of female Swiss mice as a solution in acetone three times weekly for 17 months. Acetone alone served as a solvent control, although no results were reported for this group.

chrysene occurs in complex mixtures of chemicals that may include tumor promoters, its activity as an initiating agent is noteworthy.

#### 4.3.5.5 General discussion

The only end point of toxicity that has been evaluated for chrysene is that of dermal carcinogenicity. There is some suggestion that perinatal exposure of mice by subcutaneous or intraperitoneal injection can lead to tumor formation as well (Buening et al. 1979, Grover et al. 1975, IARC 1983). The mechanism of chrysene-induced carcinogenicity is likely to be similar to that of other PAHs; namely, involving metabolic activation to reactive bay-region diol epoxides that can form adducts with DNA which lead to mutation under certain circumstances (IARC 1983).

## 4.4 INTERACTIONS WITH OTHER CHEMICALS

Most human exposures to chrysene are not to the pure compound but to particle-bound chrysene; the presence of particles is likely to affect its pharmacokinetics and carcinogenicity. Sun et al. (1982) showed that when the carcinogenic polycyclic aromatic hydrocarbon benzo[a]pyrene was particle-bound, it was cleared from hamster lungs much more slowly than a pure B[a]P aerosol, thus increasing the length of time the lungs were exposed and increasing the dose to the gastrointestinal tract as a result of mucociliary clearance. Respirable PAH-containing particulates such as diesel exhaust, when coated with the phospholipid component of a pulmonary surfactant, are genotoxic (Wallace et al. 1987). Dusts can increase the rates of pulmonary cell proliferation (Harris et al. 1971, Stenback et al. 1976, Stenback and Rowland 1979), which in turn increases the susceptibility of those cells to an initiation event in the presence of a carcinogen. Coadministration of B[a]P and particles greatly increases respiratory tract tumor yields in experimental animals (Stenback et al. 1976, Stenback and Rowland 1979). The effects of particles on potential chrysene carcinogenesis is likely to be similar.

Human exposure to chrysene in the environment seldom, if ever, occurs to chrysene alone but to chrysene as a component of complex mixtures of PAHs and other chemicals. Interactions between chrysene and other mixture components are likely to occur. In particular, interactions may play a large part in carcinogenesis resulting from experimental exposure to PAHs. For example, Mahlum et al. (1984) have shown that different temperature range distillates of coal liquids have different skin-tumor-initiating activities in mice despite the fact that they contain similar levels of known carcinogenic PAHs. This difference is believed to be because of the modifying effects of the spectrum of noncarcinogenic PAHs obtained at different temperatures. Most of the PAH components of coal liquid fractions obtained at different temperatures will vary both qualitatively and quantitatively; consequently, their abilities to modify carcinogenesis will vary accordingly. However, the relative roles of the PAH components of each of such mixtures are unknown; therefore, quantitative evaluation is not possible. Since human exposure occurs to mixtures of PAHs and not individual components, quantitative evaluation of the toxicity of individual PAHs is probably insufficient.

Human exposure to complex mixtures of PAHs has been extensive, and some adverse effects are well-documented, particularly carcinogenic effects following long-term exposure. The extent of human exposures to well-defined PAH mixtures that are responsible for producing excess disease is generally not known in quantitative terms. Coke-oven emissions and related substances such as coal tar have probably been the most widely studied. Coal tar derivatives were most likely responsible for the first observation of occupational cancer (that of scrotal cancer among London chimney sweeps) made by Percival Pott in 1775. More recent mortality studies have demonstrated strong associations between human exposure to coke-oven emissions and excess disease; specifically, significant increases in lung and genitourinary cancer mortality have been observed (IARC 1983). The earliest of these reports was made in 1936 by investigators in Japan and England (Kennaway and Kennaway 1936) who were studying lung cancer mortality among persons employed in coal carbonization and gasification processes. Subsequent studies conducted in the United States clearly demonstrated substantial increases in lung and genitourinary system cancer mortality among coke-oven workers (Lloyd 1971, Redmond et al. 1972, IARC 1984). Human tumorigenicity has also been reported as a result of exposure to creosote. Creosote is a generic term that refers to wood preservatives derived from coal tar, creosote, or coal tar neutral oil and includes extremely complex mixtures of liquid and solid aromatic hydrocarbons. Workers who engaged in activities such as dipping timbers in creosote were reported to have developed malignant and premalignant skin lesions of the face, arms, and scrotum (O'Donovan 1920, Cookson 1924, Henry 1947, Lenson 1956). Many of the individual PAH components of creosote, such as chrysene, have been shown to be both mutagenic and carcinogenic in laboratory bioassays, thus supporting the evidence of its human carcinogenicity (IARC 1983).

Exposures to many other complex chemical mixtures that include PAHs have been associated with human disease incidence, such as the use of tobacco products and exposure to roofing tar emissions and shale oils. Although this discussion falls short of providing a thorough review of the extensive literature available on the experimental and epidemiological observations of the toxicity of PAH mixtures, its purpose has been to provide examples wherein such toxicity has been documented to emphasize that human exposure occurs to multiple PAHs.

Predicting the toxicity of a complex mixture on the basis of one or several of its components may be misleading because of the possibility of interactions among the components that may modify toxicity. For example, both carcinogenic and noncarcinogenic PAHs may compete for the same metabolic activating enzymes and thereby reduce the toxicity of carcinogenic PAHs. For example, Lacassagne et al. (1945) showed that simultaneous application of chrysene and 3-methylcholanthrene to mouse skin reduced the latter's carcinogenic potency. Exposure to other PAHs may induce enzyme levels leading to more rapid detoxication of chrysene, thus reducing its carcinogenicity (Slaga and diGiovanni 1984, Weibel 1980). Naturally occurring compounds have been found to induce the enzymes that metabolize PAHs, leading to either increased or decreased toxicity. For example, plant flavonoids can induce microsomal monooxygenases and reduce the carcinogenicity of chrysene (Weibel 1980). Environmental contaminants such as TCDD can also increase microsomal

enzyme activity and consequently affect PAH toxicity (Kouri et al. 1978). Interactions can thus play important modulating roles in PAH toxicity that may not be adequately reflected in the identification of significant human exposure levels based on the toxicity of single PAHs, since human exposure occurs to mixtures of PAHs.

# 5. MANUFACTURE, IMPORT, USE, AND DISPOSAL

## 5.1 OVERVIEW

Chrysene is on the Toxic Substances Control Act (TSCA) Chemical Inventory (EPA 1979a) which lists chemicals (as defined by TSCA) that have been manufactured, imported, or processed for a commercial purpose in the United States since January 1, 1975. Data from the TSCA inventory indicate that the aggregate production of chrysene is less than 1 million pounds. Chrysene also occurs in fossil fuels and as a result of the incomplete combustion of fuel and wood. Chrysene is available as a research chemical by some specialty chemical firms. Chrysene and other aromatic hydrocarbons are found in coal tar and in the creosote oils and pitches formed from the distillation of coal tars. Coal tar pitch is primarily used as a binder for electrodes. Creosote is primarily used as a wood preservative. Coal tar is also used as a therapeutic treatment for skin diseases such as psoriasis. PAHs are also found in limited amounts in bitumens and asphalt.

## 5.2 PRODUCTION

The primary source of chrysene in air is incomplete combustion of fuel or wood for heating (EPA 1985). Chrysene also occurs in coal tar formed during the distillation of coal. Chrysene is formed in very small amounts during distillation or pyrolysis of many fats and oils. Chrysene can be synthesized by heating hydrogen and acetylene to 800°C.

Crude coal tar is produced as a by-product in the formation of coke from coal. Hot gases and vapors released from the conversion of coal to coke are collected in a scrubber that condenses these gases into ammonia, water, crude tar, and other by-products. A typical coke oven produces 80% coke, 12% coke-oven gas, 3% coal tar, and 1% crude benzene. The coal tar is then distilled to yield a number of chemical oils, creosote, and coal tar pitch. The coal tar pitch residue is 40.5% of the crude tar; creosote is ~11.5%. Heavy and light creosote also make up a small percentage of distillate (NIOSH 1977). Coal tar contains ~4 g/kg chrysene; coal tar pitch contains <10 mg/kg chrysene; and creosote oil contains <1 mg/kg chrysene (EPA 1985). This results in an annual yield of chrysene of $9.6 \times 10^3$ metric tons from coal tar, 10 metric tons from coal tar pitch, and 510 kg from creosote.

As of 1981, the world output of crude coal tar was $1.8 \times 10^7$ metric tons; $1.4 \times 10^7$ metric tons were of coke-oven origin. In 1980, the U.S. production of crude tar was $2.4 \times 10^6$ metric tons. Creosote oil production in the United States in 1981 was estimated to be $5.10 \times 10^5$ metric tons. The coal tar pitch production in the United States in 1974 was estimated to be $1 \times 10^6$ metric tons (McNeil 1983).

Bitumens and asphalt (a mixture of bitumen with mineral materials) are derived from crude oil. Bitumen samples have been reported to contain 0.2 to 34 mg/kg chrysene (IARC 1985).

## 5.3 IMPORT

In 1985, the United States imported a total of almost 12 million gallons of creosote oil from the Netherlands, France, West Germany, and other countries, and almost 185 million pounds of coal tar pitch, blast furnace tar, and oil-gas tar from Canada, Mexico, West Germany, Asian countries, Australia, and other countries (USDOC 1986).

## 5.4 USE

Chrysene has some use as a research chemical. It is available from some specialty chemical firms in low quantities (1 g) (Aldrich Chemical Co. 1986).

Coal tar pitch is primarily used as a binder for electrodes in the aluminum reduction process; it is used to bind the carbon electrodes in the reduction pots (NIOSH 1977). In North America, coal tar pitch is also used as the adhesive in membrane roofs (McNeil 1983).

Almost 99% of the creosote produced is sold to wood preservation plants; another 0.1 to 0.2% is sold to individual customers (NIOSH 1977). Creosote is used in the preservation of railroad ties, marine pilings, and telephone and telegraph poles. Some creosote is also consumed as fuel by steel producers (NIOSH 1977).

Bitumens and asphalt are used in paving, roofing, and sound and electrical insulation (IARC 1985).

## 5.5 DISPOSAL

In 1978, following input of 0.4 metric tons of chrysene from coal-tar creosote, 0.69 mg/L chrysene was found in raw water discharge from timber product industries (EPA 1985).

Total wastewater discharge of chrysene in 1978 from coke-making operations was 10 metric tons (EPA 1985).

# 6. ENVIRONMENTAL FATE

## 6.1 OVERVIEW

Chrysene in the environment is derived from both natural (e.g., wildfires, volcanoes) and man-made sources, but chrysene originating from man-made sources is quantitatively the most significant. Chrysene, like all PAHs, is formed during high-temperature pyrolytic processes. Consequently, combustion is the major source of environmental chrysene. Virtually all direct releases of chrysene into the environment are to the air. Small amounts are released to water and land. Chrysene is removed from the atmosphere by photochemical oxidation and dry or wet deposition to land or water. Chrysene that reaches the surface is likely to remain and will be partitioned primarily to soil/sediment where it is very persistent. The dominant degradation process for chrysene in soil/sediment is biodegradation. Biodegradation is a slow process; a half-life of 1,000 days has been estimated for chrysene in soil.

## 6.2 RELEASES TO THE ENVIRONMENT

Incomplete combustion of carbonaceous material is the major source of chrysene in the environment. Residential heating and open burning (man-induced and natural) are the largest combustion sources. The large quantity of chrysene released by these sources is a consequence of inefficient combustion processes and uncontrolled emissions. Of all home heating sources, wood heating is the greatest contributor to chrysene emissions. In a recent assessment of chrysene sources and release volumes across the United States, EPA (1985) estimated that home wood combustion contributed 122 metric tons or 33% of all released volumes. Open burning sources, overall, are responsible for 200 metric tons or 55% of total chrysene releases; prescribed burning is responsible for 100 metric tons of that total, wildfire for 60 metric tons, and agricultural burning for 40 metric tons. All other sources (e.g., production and use of coal tar, creosote, asphalt, and bitumen; and wastewater discharges) individually contribute 1% or less to total chrysene releases on a national scale. These releases, however, may contribute significantly to chrysene levels in certain localized areas.

Ninety-three percent of all estimated environmental releases of chrysene are to air. Of the remaining 7%, approximately equal amounts of chrysene are released to water and land.

Although they are the source of small amounts of chrysene and other PAHs on a national scale, hazardous waste sites can be concentrated sources of PAHs on a local scale. For example, abandoned wood treatment plants are sources of high concentrations of creosote, and former manufactured-gas plants (town gas sites) are sources of high concentrations of coal tar. Both creosote and coal tar are composed of a

variety of PAHs, including chrysene. PAHs at these sites are likely to occur on the soil and on suspended particulate matter in the air.

## 6.3 ENVIRONMENTAL FATE

Few data are available which describe the environmental fate of chrysene specifically, and much of the understanding of chrysene fate is based on analogy to benz[a]anthracene, benzo[a]pyrene, and PAHs, in general. The discussion below is based primarily on these generalizations.

The environmental fate of chrysene is determined to a large degree by the chemical's low water solubility and high propensity for binding to particulate or organic matter. As a result, chrysene in the atmosphere is expected to be associated primarily with particulate matter, especially soot, whereas the majority of chrysene in aquatic systems is expected to be strongly bound to suspended particles or bed sediments. Likewise, chrysene will be strongly sorbed to surface soils. Dispersion of particle-bound chrysene is the primary transport process within air, water, and land.

Based on an analogy to benzo[a]pyrene, dry deposition of particle-bound chrysene is probably the most significant transport process between air and land or water (EPA 1979b), although wet deposition is known to occur (Den Hollander et al. 1986). Because of a very low vapor pressure, chrysene that reaches the surface will likely remain and will be partitioned primarily to soils/sediments. Sediment/particle adsorption and biotic uptake are the primary transport processes for the removal of water-borne chrysene. Desorption into water from soil is very unlikely, and erosion of contaminated soils by surficial runoff is the most probable transport process for soil-bound chrysene to aquatic systems.

Information on the fate of particulate PAHs, including chrysene, released to the atmosphere is presently unclear. It is generally assumed, however, that photochemical oxidation processes play an important role. Atmospheric half-lives on the order of days have been suggested (NAS 1972). PAHs strongly absorb solar radiation at wavelengths above 300 nm, and there is sufficient evidence to indicate that PAHs undergo photooxidation in solution, as pure solids, and when adsorbed onto certain solid substrates such as alumina (NAS 1972). Singlet oxygen has been implicated as the primary oxidant, and endoperoxides and, ultimately, quinones as the reaction products (NAS 1972).

It has been inferred that similar processes take place when the compounds are adsorbed on airborne particles. Kamens et al. (1986) reported that chrysene and other PAHs adsorbed on soot particles rapidly decayed in the presence of sunlight. However, photooxidation of chrysene and other PAHs adsorbed on carbon black particles was extremely slow (Barofsky and Baum 1976). Similarly, Korfmacher et al. (1980a,b) found that benzo[a]pyrene and other PAHs that are adsorbed on fly ash are highly resistant to photodegradation. More research is needed to elucidate the rate and substrate dependency of atmospheric chrysene degradation.

Data collected by Smith et al. (1978) indicate that within aquatic systems most PAHs accumulate in the sediment and are transported with suspended sediment. PAHs, including chrysene, also accumulate in aquatic organisms. However, many organisms metabolize and excrete PAHs rapidly so that bioaccumulation is a short-term process. For example, in bluegill sunfish, an 89% loss of benzo[a]pyrene (B[a]P) was recorded 4 h after exposure (Leversee et al. 1981). Lee et al. (1972) reported rapid elimination of B[a]P in three species of California marine teleosts. Depuration rates in invertebrate species vary more widely. Some species, such as hard-shell clams, show little or no depuration, whereas others, such as many oysters, eliminate virtually all PAHs following exposure (Eisler 1987).

Aquatic organisms can also assimilate PAHs from food. For example, crustaceans and fish have been reported to readily assimilate PAHs from contaminated food (Eisler 1987). However, in many cases where assimilation of PAHs has been demonstrated, metabolism and excretion of PAHs were rapid (Eisler 1987). In laboratory aquatic ecosystem studies in which radiolabeled B[a]P was used, Lu et al. (1977) found that B[a]P can be accumulated through food to high levels in the mosquito fish. After 3 days of exposure, the intact parent compound comprised over 50% of the extractable radiolabeled carbon in fish. However, after 33 days of exposure, the intact parent compound comprised only 7% of the total extractable radiolabeled carbon, indicating extensive metabolism of B[a]P. The tendency of fish to metabolize PAHs may explain why PAHs are frequently undetected or only detected in low concentrations in the livers of fish from environments heavily contaminated with PAHs.

A minimal amount of PAHs are dissolved in the water column and degraded rapidly (half-life = several hours, EPA 1979b) by direct photolysis. Chemical oxidation may be a significant fate process for chrysene in the water column when chlorine or ozone (both oxidants) exist in sufficient concentrations (EPA 1979b).

The major fate of sediment-bound PAHs, including chrysene, is most likely biodegradation (EPA 1979b). In general, biodegradation processes are quite slow; a half-life of 7,000 h has been reported for benz[a]anthracene (EPA 1979b), and it is likely that the degradation rate for chrysene is similar. Biodegradation half-lives in contaminated streams can be 10 to 400 times longer. These long half-lives indicate that PAHs are relatively persistent in sediments and aquatic systems.

Within terrestrial systems, biodegradation is also the probable dominant fate process; however, because this process is very slow, chrysene is very persistent in soils. Bossert and Bartha (1986) reported that 84% of the original amount of chrysene applied to soils existed after 16 months of incubation with bacteria. Coover and Sims (1987) estimated a half-life of chrysene in soil of 1,000 days.

At hazardous waste sites, half-lives may be longer since other contaminants present at the site may be toxic to the degrading microorganism. Bossert and Bartha (1986) reported reduced biodegradation of chrysene in soil containing a chemical toxic to microorganisms.

# 7. POTENTIAL FOR HUMAN EXPOSURE

## 7.1 OVERVIEW

As the previous discussions indicate, the greatest portion of chrysene releases to the environment is directly into the atmosphere. Consequently, inhalation is one of the primary routes of background human exposure to chrysene in the environment. Part of the chrysene in the atmosphere returns to the surface via dry and wet deposition. This input leads to chrysene in soil and water to which humans may be exposed. Humans also may be exposed to chrysene in food, tobacco smoke, and some occupational environments, and through the use of or contact with PAH-containing products such as creosote, asphalt, and tar. At hazardous waste sites, humans will most likely be exposed to chrysene in the soil and on particulate matter in the air. At this time, chrysene has been found at 71 of the 1,177 hazardous waste sites on the National Priorities List (NPL) in the United States (View 1989).

Background exposure concentrations vary with the different media. Chrysene concentrations in air have been reported to be between 0.04 and 4.8 ng/m$^3$ (Gordon and Bryan 1973, Fox and Staley 1976). Concentrations in finished drinking water range from <1 to 8 ng/L (Sorrell et al. 1981). Daily chrysene intake via the diet has been estimated to be 3 ng (EPA 1985). Cigarette smoking and occupational exposures can add significantly to overall background exposures, because chrysene concentrations associated with these exposure pathways can be one to five orders of magnitude higher.

## 7.2 LEVELS MONITORED IN THE ENVIRONMENT

### 7.2.1 Air

Very little data are available to characterize chrysene levels in air, and estimates of ambient concentrations are limited to a small number of relatively outdated monitoring studies in Los Angeles, Baltimore, and Pittsburgh. Consequently, definitive statements about average background exposure levels cannot be made. In the most recent monitoring study, Gordon (1976) reported ambient chrysene concentrations in Los Angeles County to range between 0.36 and 1.02 ng/m$^3$. This is somewhat lower than the values reported by Gordon and Bryan (1973), also in Los Angeles County. Based on monitoring data from 1971-1972, they reported chrysene levels in the range of 0.04 to 3.8 ng/m$^3$. During the same time period, Fox and Staley (1976) reported average chrysene concentrations of 4.8 ng/m$^3$ in College Park, Maryland. A much higher average concentration of 106 ng/m$^3$ was reported in the Baltimore Harbor Tunnel in Baltimore, Maryland. DeMaio and Corn (1966) reported chrysene concentrations in Pittsburgh of approximately 5 ng/m$^3$.

### 7.2.2 Water

Chrysene has been detected in raw and finished drinking waters in the United States, but minimal data limit the degree to which background levels can be adequately characterized. Sorrell et al. (1981) reported chrysene concentrations between 4 and 9 ng/L in raw water, and from <1 to 8 ng/L in finished drinking water. These data were based on very small samples (10 cities) and may not be representative of drinking water concentrations in the United States. Because of a high propensity to bind to organic matter, it is unlikely that chrysene will occur to any appreciable extent in surface water or groundwater at hazardous waste sites or other areas.

### 7.2.3 Soil

No data are available on chrysene levels in U.S. soils. Blumer et al. (1977) summarized data on the concentrations of total PAHs in soil and reported values between 4 and 13 mg/kg in the soil from relatively rural areas of the eastern United States. Soils in more populated and industrialized areas may have higher levels. Butler et al. (1984) examined soil PAH levels in Switzerland and demonstrated much higher soil chrysene concentrations near complex road interchanges than at areas more distant. Also, the soils at waste sites, such as former manufactured-gas plants and creosote-wood treatment plants, may contain high levels of PAHs, including chrysene.

### 7.2.4 Food

Chrysene has been detected in vegetables (up to 395 μg/kg), oils and fats (up to 200 μg/kg), and roasted coffee (3.0 to 19.1 μg/kg) (IARC 1983). Chrysene has also been detected in charcoal-broiled steak at a level of 1.4 μg/kg (Lijinsky and Shubik 1964). The amount of chrysene in meat depends on the method of cooking; time of exposure, distance from the heat source, and the disposal of fat during cooking all influence chrysene content.

Chrysene has also been detected in vegetables and fruits grown in PAH-contaminated soil near high traffic areas at levels of 0.7 to 22 μg/kg (Wang and Meresz 1982). Thus, consumption of food grown near contaminated areas such as roadways, industrial areas, or hazardous waste sites may contribute to human exposure.

Humans may also be exposed to chrysene and other PAHs found in aquatic organisms that are typical components of the diet. Specifically, PAHs have been detected in bivalve mollusks (i.e., clams, oysters, mussels), crabs, and lobsters (Eisler 1987). PAHs have also been detected in fish, but fish levels are usually low because fish rapidly metabolize PAHs.

### 7.2.5 Cigarette Smoke

Chrysene has been reported to occur in cigarette mainstream smoke at between 6 and 96 ng per cigarette (IARC 1983). Concentrations of chrysene in sidestream smoke may be higher, since levels 2 to 4 times higher have been reported for other PAHs (DHHS 1986). Thus, involuntary

smokers, in addition to smokers, may receive elevated exposures to chrysene from cigarettes.

## 7.3 OCCUPATIONAL EXPOSURES

PAHs, such as chrysene, have been isolated in numerous occupational situations, including coal tar production and coking plants, coal gasification sites, smoke houses, aluminum production plants, asphalt and bitumen production plants, road and roof-tarring activities, and around municipal incinerators. Historically, the highest level of human exposure to PAHs occurred in industrial situations; concentrations of benzo[a]pyrene (often used as an indicator of total PAH concentration) have been reported to range from 800 to 23,100 $ng/m^3$ in the workroom air of coke-oven operations in the United Kingdom (Davies et al. 1986). Similar high values have been reported by Lindstedt and Sollenberg (1982) in Swedish industries.

## 7.4 POPULATIONS AT HIGH RISK

At highest risk for cancer are those people who are exposed to high levels of PAHs. Examples of high-risk populations include workers in certain occupations that have elevated PAH concentrations in the ambient work environment; smokers and involuntary (passive) smokers who receive elevated PAH intake through tobacco smoke; and populations living near industries, such as creosote and coal tar manufacturers, that generate PAHs as a by-product of production.

Individuals in these high-exposure groups may have varying susceptibilities to PAH toxicity. Some of the available data on PAH carcinogenicity suggest a relationship between aryl hydrocarbon hydroxylase (AHH) activity and cancer risk. Genetic variation in AHH inducibility has been implicated as a determining factor for susceptibility to lung and laryngeal cancer (EPA 1980). Attempts have been made to demonstrate that persons with lung cancer have higher inducibility of AHH in cultured lymphocytes. A review by Calabrese (1984) indicates that several studies support this hypothesis, and some genetic data indicate that the human population can be segregated based on this trait (EPA 1980). Thus, individuals that are AHH-inducible may constitute a high-risk population. However, the data regarding genetic susceptibility are not yet conclusive.

# 8. ANALYTICAL METHODS

## 8.1 ENVIRONMENTAL SAMPLES

The procedures used to sample and extract chrysene in different media are very similar. In air and tobacco smoke, PAHs, including chrysene, are adsorbed predominantly on particulate matter, which is collected on a filter. In water and soil, PAHs are extracted without filtration.

The extraction of PAHs from the filter can be accomplished by a variety of techniques with or without solvents. The following extraction methods are the most commonly used techniques: Soxhlet, sublimation at elevated temperatures, ultrasonic, and polytron extraction (Sawicki 1976).

A cleanup step is necessary to separate chrysene and PAHs from other pollutants. Typically, this step involves liquid-liquid extraction of the dry organic particulate extract followed by adsorption chromatography using silica gel or alumina columns (Sawicki 1976, Riggin and Strup 1984). These adsorbents selectively remove interfering compounds. In addition, thin-layer chromatography (TLC) can be used as a cleanup method (Sawicki 1976).

The most commonly used analytical methods for determining chrysene in environmental samples are column gas chromatography (GC) and high-performance liquid chromatography (HPLC). Table 8.1 summarizes common analytical methods, detection limits, and accuracy (percent recovery) for the determination of chrysene in air, water, soil, and food.

GC is an analytical technique in which components of a sample are separated by differential distribution between a gaseous mobile phase and a solid or liquid stationary phase (EPA 1983). Following separation in the GC column, sample components are identified and quantified by a detection system such as flame ionization detection (FID), ultraviolet absorption spectroscopy (UV), or mass spectrometry (MS). These techniques are detailed in NIOSH (1984) and EPA (1983, 1984a).

HPLC is an analytical method in which components are separated based on their polarity (EPA 1983). Reverse-phase HPLC, which is used more widely for the analysis of PAHs, uses a nonpolar stationary phase and a polar mobile phase; hydrophilic components are eluted earlier than hydrophobic components. The detection systems most appropriate for HPLC analysis of PAHs are UV absorption spectroscopy and fluorescence spectroscopy (FS). Das and Thomas (1978) examined the use of both a UV and a fluorescence detector for determining PAHs following HPLC. The UV detection system failed to resolve chrysene from benz[a]anthracene in a multicomponent mixture. However, by selection of excitation and

**Table 8.1. Methods for analysis of chrysene in environmental media**

| Media | Sample preparation | Analytical method[a] | Detection limit | Accuracy[b] | References |
|---|---|---|---|---|---|
| Air | Ultrasonic extraction with cyclohexane | HPLC | 3 ng/m$^3$ (1500-m$^3$ sample) | 95% | NIOSH 1984 (Method 5506) |
| | Ultrasonic extraction with benzene, pentane, or dichloromethane | HPLC/FS | 50 pg | NA | Andersson et al. 1983 |
| | Extraction with solvent | GC/MS | NA | NA | NIOSH 1984 (Method 5515) |
| | Soxhlet extraction with dichloromethane | TLC/FS | 0.1 ng/g suspended particulate matter | NA | Katz 1979 |
| Water | Extraction with methylene chloride | HPLC/FS | 0.15 $\mu$g$^3$/L | ~77%[c] | EPA 1984a (Method 610) |
| | | UV | 4 $\mu$g/L | 76–135% | Riggin and Strup 1984 |
| | Extraction with methylene chloride at pH <2 and pH >11 | GC/MS | 2.5 $\mu$g/L | ~93%[c] | EPA 1984a (Method 625) |
| | Extraction with methylene chloride at pH 12–13 and pH <2 | GC/MS | 10 $\mu$g/L | NA | EPA 1984a (Method 1625) |
| | | GC/MS | NA | NA | EPA 1986a |
| | Extraction with dichloromethane | HPLC/UV | 70 pg | NA | Ogan et al. 1979 |
| | Extraction with cyclohexane | TLC/FS | 0.5–1 ng/L | NA | Borneff and Kunte 1979 |
| Soil | Extraction with *n*-pentane | TLC/UV | NA | NA | Butler et al. 1984 |
| | Extraction with methylene chloride | GC/MS | NA | NA | NIOSH 1984 |
| Food | Extraction with isooctane | TLC/UV | 0.2 $\mu$g/kg | NA | Howard 1979 |

[a]Abbreviations: HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography; FS, fluorescence spectroscopy; GC, gas chromatography; MS, mass spectrometry; UV, ultraviolet absorption spectroscopy.

[b]NA = not available.

[c]In large samples.

emission wavelengths, FS can obtain resolution of both chrysene and benz[a]anthracene.

Thin-layer chromatography (TLC) has also been used to analyze for PAHs. With quasi-linear luminescence methods (QLL), quasi-linear spectra can be obtained for PAHs at liquid nitrogen temperatures (Sawicki 1976).

GC and HPLC are the chromatographic methods routinely used for the determination of 10 to 20 of the major PAHs in air and water samples. Detailed analysis of major and minor PAHs in a complex PAH mixture requires a combination of chromatographic techniques (Wise et al. 1986). Gas chromatography/mass spectrometry (GC/MS) has a detection limit of greater than 10 pg; HPLC/FS has an approximate detection limit for PAHs of 25 to 50 pg (Santodonato et al. 1981). Das and Thomas (1978) reported a detection limit (twice the signal-to-noise ratio) of 2.3 pg for chrysene from a synthetic PAH mixture following HPLC/FS.

HPLC (5506) or GC/MS (5515) are the methods recommended by NIOSH for analyzing chrysene in workplace air (NIOSH 1984). These methods incorporate a sampling train consisting of a filter and a solid sorbent (NIOSH 1984). The use of a high-volume sampler to sample a large quantity of air allows for the detection of small amounts of PAH. The analytical methods required by EPA (1984a) for the analysis of chrysene in water are procedures 610 (HPLC/FS), 625 (GC/MS), and 1625 (GC/MS). These are required test procedures for municipal and industrial wastewater-discharging sites under the Clean Water Act. GC/MS is the method required by the EPA Contract Laboratory Program for analysis of chrysene and other PAHs in water and soil. The Contract Required Quantitation Limit (CRQL) for chrysene in water is 10 µg/L (EPA 1986a); in soil/sediment, the limit is 330 µg/kg.

## 8.2 BIOLOGICAL SAMPLES

The available biological monitoring techniques are useful for detecting whether occupational or environmental exposure to PAHs has occurred, but because there have been no population-based studies to determine normal body levels of PAHs, it is not yet possible to predict environmental exposure from body PAH levels or to predict what health effects are likely to be associated with these levels. In general, techniques that measure PAH or PAH metabolite concentrations in the urine are most appropriate for use in determining occupational exposure, since a high level of PAH exposure is necessary to result in the presence of these compounds in the urine. Methods that detect diol epoxide-DNA adducts are more sensitive to low exposure levels and are most appropriate for use in determining environmental exposure. The techniques presently available for determining exposure to PAHs are summarized in Table 8.2 and discussed in detail below.

Modica et al. (1982) and Bartosek et al. (1984) examined PAHs present in blood, mammary, adipose, liver, and brain tissue from rats using gas-liquid chromatography with a flame-ionization detector. Chrysene was determined in all tissues examined. Examples of chrysene concentrations in human tissue samples using this technique were not located in the available literature. The detection limit for this method was not reported.

**Table 8.2. Methods for analysis of PAHs in biological samples**

| Medium | Technique | Measured parameter | Reference |
|---|---|---|---|
| Tissue | Gas chromatography | PAH concentration | Modica et al. 1982, Bartosek et al. 1984 |
| | High-performance liquid chromatography | PAH diol epoxide-DNA adducts | Mushtaq et al. 1987 |
| | Postlabeling of DNA | PAH diol epoxide-DNA adducts | Randerath et al. 1985, Randerath et al. 1986 |
| Blood | Immunoassay | Antibodies to diol epoxide-DNA adducts | Harris 1985a, Harris et al. 1986 |
| Urine | Gas chromatography | PAH concentration | Clonfero et al. 1986 |
| | High-performance liquid chromatography | PAH concentration | Becher and Bjorseth 1983, Becher et al. 1984 |

In mammalian systems, chrysene is converted by specific cellular enzymes to *trans*-dihydrodiols. These dihydrodiols are further converted to diol epoxides that are capable of binding to DNA (Phillips et al. 1986). HPLC was used to determine radiolabeled chrysene diol epoxide adducts to DNA formed in vitro (Mushtaq et al. 1987). These techniques have not been examined in humans or in actual biological samples to determine if abnormal levels can be detected.

Randerath et al. (1985, 1986) examined PAH-DNA adducts in skin tissue from mice dermally treated with cigarette smoke condensate, also in human placenta, bronchus, and larynx tissue from smokers. In this technique, radioactivity ($^{32}P$) is incorporated into the DNA removed from the exposed cells, and the digested DNA is separated using TLC. Quantitation of the adducts is achieved by scintillation counting. Small amounts of DNA are needed for analysis. These techniques have not been examined in humans or in actual biological samples to determine if abnormal levels can be detected.

Procedures are currently available to examine the presence of antibodies to PAH-DNA adducts in the blood using enzymatic immunoassays (Harris 1985a, Harris et al. 1986). Harris et al. (1986) examined human sera from coke-oven workers, individuals exposed to ambient levels of PAHs, and individuals with carcinoma of the lung, for the presence of antibodies to PAH-DNA adducts, including chrysene-DNA adducts. Positive sera contained antibodies to each PAH individually or to epitopes common to the PAHs. Positive sera was found in 25% of the coke-oven workers, in 33% of the control individuals, and in 57% of the cancer patients. However, because of the high percentage of control individuals with positive sera, the sensitivity of the technique may be limited. Harris (1985a) developed a technique for determining human exposure to PAHs by using immunoassay to detect antibodies in sera to diol epoxide-DNA adducts. The technique was tested on coke-oven workers exposed to substantial amounts of benzo[a]pyrene in the work atmosphere and on smokers and nonsmokers. Antibodies to benzo[a]pyrene diol epoxide-DNA adducts were quantified by enzyme-linked immunosorbent assay (ELISA). Higher proportions of sera positive for antibodies were found in a group of smokers and in the occupationally exposed group.

The urine of exposed humans was also examined for the presence of chrysene. PAHs can be extracted from urine and analyzed using HPLC/FS or GC/MS (Becher and Bjorseth 1983, Becher et al. 1984, Clonfero et al. 1986). Chrysene was found in the urine of workers exposed to PAHs in an aluminum plant. However, environmental exposure could not be determined from urine chrysene content because high atmospheric concentrations of PAHs in the workplace were not found to be reflected to the same extent in excretion of PAHs in the urine (Becher et al. 1984). Clonfero et al. (1986) detected chrysene using GC/MS on the urine of individuals treated therapeutically with crude coal tar. However, this is not necessarily a useful test for occupational or environmental exposure, because high levels of PAHs in the coal tar were necessary to concentrate PAHs in the urine.

Vo-Dinh et al. (1987) developed an antibody-based fiber-optics biosensor that can be used to detect benzo[a]pyrene or other PAHs in sample solutions. In this technique, antibodies to benzo[a]pyrene are

covalently bound to the tip of the sensing probe. A helium-cadmium laser excites the molecules of benzo[a pyrene bound to the antibodies, and the resulting fluorescence of these molecules is recorded by a photomultiplier; the intensity of the fluorescence signal is proportional to the amount of antigen bound to the sensor tip. The fiber-optics device can detect 1 femtomole (fmol; one-quadrillionth of a mole) benzo[a]pyrene in a 5-μL sample drop. This technique can be useful in the assessment of an individual's exposure to benzo[a]pyrene and other PAHs, provided appropriate antibodies are used.

# 9. REGULATORY AND ADVISORY STATUS

Regulatory standards have been developed for the carcinogenic PAHs in a benzene or cyclohexane soluble fraction of coal tar pitch volatiles. However, the regulatory standards were developed to regulate exposures to all PAHs in coal tar pitch volatiles and are appropriate for chrysene. These standards and advisory guides are presented in Table 9.1.

Chrysene has been shown to be carcinogenic in experimental animals and undergoes metabolism to reactive electrophiles capable of binding covalently to DNA and inducing bacterial mutation and DNA damage. IARC (1973) has classified chrysene in Group 2B because of limited evidence of carcinogenicity in experimental animals. IARC (1985) has also concluded that there is sufficient evidence of the carcinogenicity of coal tars, creosote, and coal tar pitches in experimental animals. In addition, IARC concluded that there is sufficient evidence that occupational exposure to coal tar and coal tar pitch is associated with skin cancer and limited evidence of the carcinogenicity of creosote in occupationally exposed individuals.

## 9.1 INTERNATIONAL

The World Health Organization European standards for drinking water recommend a concentration of PAHs not to exceed 0.2 μL. This is based on the composite of six PAHs in drinking water: fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, benzo[b]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-cd]pyrene (WHO 1971). This limit was not chosen on the basis of potential health effects.

## 9.2 NATIONAL

### 9.2.1 Regulatory Standards

Coal tar, coal tar pitch, and creosote are considered by NIOSH and EPA to be human carcinogens (NIOSH 1977; EPA 1978, 1981, 1984c, 1986b). NIOSH reviewed epidemiologic and experimental toxicological evidence and concluded that inhalation exposure to these coal products, which contain a number of PAHs, increases the risk of lung and skin cancer in workers (NIOSH 1977). The Secretary of Labor has taken the position that no safe occupational exposure can be established for a carcinogen.

The current workroom air standard determined by OSHA is an 8-h time-weighted average permissible exposure limit (PEL) of 0.2 $mg/m^3$ for the benzene-soluble fraction of coal tar pitch volatiles. The PEL was established to minimize exposure to those volatiles believed to be carcinogens; these include benzo[a]pyrene, anthracene, phenanthrene, acridine, chrysene, and pyrene (OSHA 1986).

**Table 9.1. Regulatory standards and advisory levels**

| Regulatory standard or advisory level | Basis | Concentration or risk coefficient | Reference |
|---|---|---|---|
| | **Air** | | |
| Regulatory standard | | | |
| 8-h Time-weighted average permissible exposure limit (PEL) | Benzene-soluble fraction of coal tar pitch volatiles | 0.2 $\mu g/m^3$ | OSHA 1985 |
| Advisory levels | | | |
| 8-h Time-weighted average threshold limit value | Benzene-soluble fraction of coal tar pitch volatiles | 0.2 $\mu g/m^3$ | ACGIH 1986 |
| 10-h Time-weighted average threshold limit value | Cyclohexane-soluble fraction of coal tar pitch volatiles | 0.1 $\mu g/m^3$ | NIOSH 1977 |
| | **Water** | | |
| Advisory levels | | | |
| Ambient water quality criterion | Total carcinogenic PAHs | 0 (28, 2.8, and 0.28 ng/L)[a] | EPA 1980 |

[a]The EPA recommended concentration for ambient water is zero; however, because attainment of this level may not be possible to achieve, the EPA estimated concentrations of total carcinogenic PAHs for ambient water corresponding to $10^{-5}$, $10^{-6}$, and $10^{-7}$ upper-bound lifetime excess risk estimates, respectively, are presented.

### 9.2.2 Advisory Levels

#### 9.2.2.1 Air advisory levels

**ACGIH time-weighted average threshold limit value.** The American Conference of Governmental Industrial Hygienists (ACGIH 1986) recommended a time-weighted average threshold limit value (TLV) for occupational exposure to coal tar pitch volatiles based on an 8-h workday and a 40-h week. The ACGIH time-weighted average TLV of 0.2 $mg/m^3$ is based on the benzene-soluble fraction of coal tar pitch volatiles, including benzo[a]pyrene, anthracene, phenanthrene, acridine, chrysene, and pyrene. The TLV is based on the ACGIH conclusion that, at concentrations below 0.2 $mg/m^3$, any increase in the incidence of lung and other tumors caused by occupational exposure to coal tar pitch volatiles should be minimal.

**NIOSH time-weighted average threshold limit value.** The National Institute for Occupational Safety and Health (NIOSH) examined the epidemiologic and experimental toxicological evidence on coal tar, coal tar pitch, and creosote, and concluded that they are carcinogenic to experimental animals and potentially to humans (NIOSH 1977). Polynuclear hydrocarbons have been identified in coal tar products. Because of the carcinogenic potential of these compounds, NIOSH recommended that the permissible exposure limit be set at the lowest concentration detected by the NIOSH-recommended method of environmental monitoring, 0.1 $mg/m^3$ (NIOSH 1977). NIOSH proposed this time-weighted average threshold limit value to reduce the risk of cancer associated with exposure to coal tar products in the work place.

#### 9.2.2.2 Water advisory levels

**Ambient water quality criterion.** EPA (1980) developed an ambient water quality criterion (AWQC) to protect human health from the potential carcinogenic effects caused by exposure to carcinogenic PAHs through ingestion of contaminated water and contaminated aquatic organisms.

Chrysene is an animal carcinogen. Because there is no recognized safe concentration for a human carcinogen, EPA (1980) recommended that the concentrations of total carcinogenic PAHs in water be zero. However, EPA (1980) recognized that a zero concentration level may not be possible to attain. The present criteria for total carcinogenic PAHs are based on the carcinogenicity assay reported by Neal and Rigdon (1967), in which stomach tumors developed in CFW-Swiss mice exposed to doses of 1 to 250 ppm benzo[a]pyrene in the diet, with a statistically higher incidence than controls. Assuming that an individual consumes 2 L of water and 6.5 g of fish and shellfish each day, the sum of the concentrations of total carcinogenic PAHs corresponding to upper-bound lifetime excess cancer risks of $10^{-5}$, $10^{-6}$, and $10^{-7}$ are 28, 2.8, and 0.28 ng/L, respectively.

#### 9.2.2.3 Food advisory levels

No food advisory levels for chrysene were found in the available literature.

#### 9.2.2.4 Other guidance

Sections 103(a) and 103(b) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) require that persons in charge of vessels or facilities from which a hazardous substance has been released in quantities that are equal to or greater than its reportable quantity (RQ) immediately notify the National Response Center of the release. Potential carcinogens are grouped into high-, medium-, or low-hazard categories on the basis of biological information available. The RQ for chrysene is 1 lb (EPA 1987).

### 9.2.3 Data Analysis

#### 9.2.3.1 Carcinogenic potency

Although EPA previously published inhalation and oral cancer risk estimates for benzo[a]pyrene (EPA 1984b), based on the studies of Thyssen et al. (1981) and Neal and Rigdon (1967), these numbers are currently under review and have not been included here pending recalculation.

## 9.3 STATE

The state of New York has recommended a guidance level of 0.2 μg/L for the sum of benz[a]anthracene, benzofluoranthenes, benzo[a]pyrene, chrysene, fluoranthene, indeno[1,2,3-cd]pyrene, methylbenz[a]anthracene, and pyrene in ambient water (NYSDEC 1984). (Regulations and advisory guidance from the states were still being compiled at the time of printing.)

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## 11. GLOSSARY

Acute Exposure--Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Bioconcentration Factor (BCF)--The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

Carcinogen--A chemical capable of inducing cancer.

Ceiling value (CL)--A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure--Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity--The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

Frank Effect Level (FEL)--That level of exposure which produces a statistically or biologically significant increase in frequency or severity of unmistakable adverse effects, such as irreversible functional impairment or mortality, in an exposed population when compared with its appropriate control.

EPA Health Advisory--An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)--The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure--Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity--The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro--Isolated from the living organism and artificially maintained, as in a test tube.

In vivo--Occurring within the living organism.

Key Study--An animal or human toxicological study that best illustrates the nature of the adverse effects produced and the doses associated with those effects.

Lethal Concentration(LO) ($LC_{LO}$)--The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration(50) ($LC_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose(LO) ($LD_{LO}$)--The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose(50) ($LD_{50}$)--The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lowest-Observed-Effect Level (LOEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

Malformations--Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level--An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen--A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity--The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-Observed-Effect Level (NOEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of effects seen between the exposed population and its appropriate control.

Permissible Exposure Limit (PEL)--An allowable exposure level in workplace air averaged over an 8-h shift.

$q1^*$--The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The $q1^*$ can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually $\mu g/L$ for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD)--An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)--The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

Reproductive Toxicity--The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL)--The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity--This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen--A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)--A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA)--An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

Uncertainty Factor (UF)--A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

## APPENDIX: PEER REVIEW

A peer review panel was assembled for chrysene. The panel consisted of the following members: Dr. James S. Felton, Lawrence Livermore National Laboratory; Dr. Dietrich Hoffman, Naylor Dana Institute, American Health Foundation; and Dr. Alexander Wood, Roche Institute of Molecular Biology. These experts collectively have knowledge of chrysene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.